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SOME PHARMACOLOGICAL PROPERTIES OF SERUM WITH SPECIAL REFERENCE TO ITS USE AS A BLOOD SUBSTITUTE.¹

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THE choice of a suitable blood substitute for transfusion purposes has assumed great importance within recent years. Experimental work (Rous and Wilson,⁽¹⁾ Levinson, Neuwelt and Necheles,⁽²⁾ Magladery, Solandt and Best⁽³⁾) has indicated that in wound shock or hæmorrhage, except when gross loss of circulating hæmoglobin has occurred, restoration of the blood volume is of much greater moment than the replacement of the red cells. Accordingly removal of the formed elements from blood by the production of either plasma or serum has made possible the use of a blood substitute, which can be stored for a long time and made available without delay for transfusion purposes.

There has been considerable discussion on the relative merits of plasma and serum. In Hamilton Bailey's recent text-book,⁽⁴⁾ the statement is made that "serum is definitely inferior to plasma". This statement probably has its origin in some reports, based on the one hand on clinical experience (Aldrich *et alii*,⁽⁵⁾ Black,⁽⁶⁾ Strumia, Wagner and Monaghan⁽⁷⁾), and on the other hand on animal experiments (Buttle, Kekwick and Schweitzer,⁽⁸⁾ Levinson, Neuwelt and Necheles⁽⁹⁾). Nevertheless considerable numbers of serum transfusions have been given both to man and to laboratory animals without injurious effects and with satisfactory therapeutic results (Bond and

Wright,⁽¹⁰⁾ Wright, Bond and Hughes,⁽¹¹⁾ Clegg and Dible,⁽¹²⁾ Magladery, Solandt and Best,⁽³⁾ Best and Solandt,⁽¹³⁾ Hill, McMichael and Sharpey-Schafer⁽¹⁴⁾); Best and Solandt⁽¹⁵⁾ state that serum is in no way inferior to plasma.

In the making of a choice between plasma and serum, the points to be considered are (i) the relative ease with which satisfactory material can be prepared, (ii) the physical character of the fluids, and (iii) the presence and amount of pharmacologically active substances which may be responsible for undesirable reactions.

From the technical point of view, the main advantage of serum over plasma is the greater ease with which it can be filtered. It is generally considered impracticable to filter plasma, and sterility must be ensured by rigid precautions during preparation. There is little to choose between the two fluids in regard to the physico-chemical qualities needed by a blood substitute, of which colloid osmotic pressure and viscosity are the most important. The slight difference in osmotic pressure due to the absence of fibrinogen in serum is of no practical significance.

The main controversy has turned on the question as to whether certain pharmacologically active substances that may be present in serum are of importance in the production of undesirable reactions. The presence of such pharmacologically active substances has long been known; the earlier work is reviewed by Janeway, Richardson and Park⁽¹⁶⁾ and the more recent papers by Amberson.⁽¹⁷⁾ The following properties have been described.

1. A vasoconstrictor and smooth-muscle stimulating action has been noted. Meyer⁽¹⁸⁾ considered that this was due to adrenaline; but O'Connor,⁽¹⁹⁾ in 1912, showed that this was not the case, clearly establishing that the active substances were formed during clotting, and caused constriction of the coronary artery as well as contraction

¹ This work was carried out with the aid of a grant from the National Health and Medical Research Council.

of various smooth-muscle preparations which were relaxed by adrenaline.

2. Adenyl compounds have been prepared from fresh serum (Zipf,¹⁰⁰ Fiske¹⁰¹). These substances are vasodilator in action and have been shown to be partly responsible for the toxicity to laboratory animals of fresh defibrinated blood or serum.¹⁰²

3. Serum (both homologous and heterologous), but not plasma, has been shown by Brodie¹⁰³ (1900) to cause respiratory disturbance and a profound depressor action on the systemic blood pressure of the cat when injected intravenously.

Recently, at the Walter and Eliza Hall Institute, we have investigated these pharmacological properties of serum; an account of this work appears more fully elsewhere (Reid and Bick¹⁰⁴). This present paper is concerned with an account of the origin of these pharmacologically active substances, the means of determining their presence and the method of preparing serum which contains them in minimal amounts. Their importance or otherwise from the point of view of human transfusions will also be discussed.

Methods.

Preparation of Serum.

Altogether about 120 samples of human serum varying in age from twelve hours to several weeks have been tested. Most of them were prepared by one of us (M.B.) at the Walter and Eliza Hall Institute, and the others came from the Commonwealth Serum Laboratories. The latter contained merthiolate (1:10,000).

1. Some samples were prepared from whole blood collected without anticoagulant, clotted at room temperature and transferred after six hours to the refrigerator (0° to 3° C.) for a further 18 hours before removal of the serum.

2. Serum was also prepared by a modification of the method described by Morgan,¹⁰⁵ in 1927, in which serum is prepared by the addition of calcium chloride in calculated amount to oxalated plasma. Such oxalated plasma was prepared by separation of formed elements from the blood, (i) by gravity over a period of twenty-four hours, (ii) by high speed centrifugation, or (iii) by separation in a modified cream separator. Sometimes citrated plasma containing 0.4% sodium citrate was used and converted to serum by the addition of $\frac{1}{10}$ of its volume of 20% calcium chloride solution. Plasma prepared by high speed centrifugation has been termed, for convenience, "platelet free" plasma.

3. Some samples of serum prepared by one or other of these methods were dried for us by Mr. Holden, by the method of Flosdorf and Mudd.¹⁰⁶

4. Serum prepared from whole blood was also dried by the method of Hardy and Gardiner.¹⁰⁷ By this method the serum, after first being concentrated to half its volume in "Cellophane" tubes placed in a draught of warm, dry air, had its proteins precipitated by being poured into 10 volumes of a mixture of seven parts of ethyl alcohol (99.5%) and three parts of anhydrous ether at -12° to -14° C. The precipitate, after standing for three hours in the cold, was washed aseptically with 10 volumes of ether by a method elsewhere described (Bick) and dried *in vacuo* over sulphuric acid.

It can be seen that these methods include the methods of preparation which are at present in common use—that is, (i) serum prepared from whole blood, (ii) serum prepared from centrifuged plasma, (iii) serum prepared from "cream-separated" plasma, (iv) serum prepared from whole blood and dried by the method of Flosdorf and Mudd, (v) "Hardyized" serum protein.

Test Objects.

For investigation of the vasoconstrictor property of serum we used the isolated spiral strip of ox carotid (modified from Meyer¹⁰⁸) suspended in Ringer's solution in an organ bath containing 10 cubic centimetres at 37° C., contraction being recorded on a smoked drum by a frictionless lever magnifying ten times. We also tested the vasoconstrictor effect of serum injected into the isolated rabbit's

ear perfused with Ringer's solution, the outflow being measured in drops per minute. For investigation of the muscle-stimulating action of serum, the isolated jejunum of the guinea-pig was used. The detailed description of these methods appears elsewhere.¹⁰⁹ The ox carotid and guinea-pig jejunum were the most suitable preparations and gave closely parallel results. Effects on these test objects cannot be due to such causes as viscosity changes or the presence of particulate matter, both of which might produce changes in the outflow from perfusion preparations such as the rabbit's ear. To detect the presence of adenyl compounds, the heart of the atropinized guinea-pig (Drury, Lutwak-Mann and Solandt¹¹⁰) was used.

The effect of the intravenous injection of homologous and of heterologous serum into cats, rabbits and dogs was investigated. The animals were anesthetized with ten cubic centimetres of 1% chloralose solution per kilogram of body weight given intravenously, the dogs being premedicated with morphine (10 to 15 milligrammes per kilogram). The lungs were artificially ventilated. The carotid blood pressure was recorded and in some experiments the pulmonary arterial blood pressure (by the method of Kellaway and Le Messurier¹¹¹) and the pulmonary venous pressure were also recorded. Injections of serum were given to intact animals, to animals with divided vagi, to atropinized, to decapitated, or to pithed animals. The effect of serum when injected into the Ringer's solution perfusing the isolated mesentery of the cat and the isolated heart of the cat (Gunn's,¹¹² 1913 modification of Langendorff's method) was determined.

The Vasoconstrictor and Smooth Muscle Stimulating Properties of Serum.

The presence of a smooth muscle stimulating and vasoconstrictor substance (or substances) in serum prepared by the clotting of whole blood was regularly demonstrable. For the purpose of comparing the activity of various samples of serum, a standard serum was employed. This was prepared by clotting whole blood and drying the serum so obtained by the method of Flosdorf and Mudd. Small samples were reconstituted with distilled water immediately before use.

Of a large number of samples of serum prepared from whole blood, all showed activity on the isolated gut or ox carotid preparation, varying within 30% above or below that of the standard serum. Such serum in doses of 0.2 to 1.0 cubic centimetre added to the Ringer's solution in the isolated organ bath of 10 cubic centimetres volume caused contraction of the guinea-pig jejunum after a latent period varying from ten to four seconds. After the serum had been in contact with the preparation for thirty seconds the Ringer's solution in the bath was changed, whereupon relaxation was rapid. The usual type of response can be seen from Figure II. Doses of serum ranging from 0.5 to 2.0 cubic centimetres caused contraction of the ox-carotid spiral after a latent period varying from thirty to three seconds. Frequently a dose of two cubic centimetres caused a maximal contraction. Usually the Ringer's solution in the bath was changed ninety seconds after the injection of serum, whereupon relaxation occurred slowly, the lever returning to the base line in from ten to twenty minutes. Doses of one cubic centimetre injected into the Ringer's solution perfusing the isolated rabbit's ear, just proximal to the cannula, nearly always caused constriction lasting from five to thirty minutes.

Such activity as that described is not due to the use of a serum foreign to the animal that supplied the test object, because it occurs when homologous serum is used,^{109, 113, 114} and, moreover, as will be seen later, the activity of serum may be modified or abolished according to the mode of preparation. We also showed that differences in activity of various samples of serum could not be due to differences in ionic content. This was done by estimating the calcium and potassium content of specimens of serum undergoing comparison and by making adjustments as necessary by the addition of calcium chloride or potassium chloride.

Plasma or whole blood possesses none of these properties. In experiments to demonstrate this, citrated plasma was

compared with serum from whole blood to which citrate was added, or whole blood, taken straight from a vein, injected into the organ bath and left in contact for thirty seconds, was compared with its corresponding serum in equivalent dosage. With longer contact, frequently contraction of the preparation occurred after a latent period of three-fourths of a minute—presumably due to the clotting process occurring in the organ bath.

Source of the Vasoconstrictor and Muscle-Stimulating Substances.

By different methods of preparation of samples of serum from the same source of blood, we clearly showed that the activity of serum depended upon the number of platelets present in the plasma at the time of clotting. For instance, serum prepared from plasma centrifugated at high speed (containing only 1,000 to 2,000 platelets per cubic millimetre) was devoid or almost devoid of activity, whereas that prepared from gravity prepared plasma (containing 200,000 to 400,000 platelets per cubic millimetre) was nearly as active as that prepared from the whole blood. "Cream-separated" plasma had a platelet count varying from 50,000 to 150,000 per cubic millimetre. Serum prepared from such plasma was not devoid of activity, but its activity was usually only one-quarter to one-third that of the standard. Figure I shows the effect of two cubic centimetre doses of differently prepared samples of serum on the ox carotid. All these samples were from the same batch of blood. At D two cubic centimetres of serum from whole blood, at B and C two cubic centimetres of serum from centrifugated plasma (2,000 platelets per cubic millimetre) and at A two cubic centimetres of serum from gravity prepared plasma (300,000 platelets per cubic millimetre) were given. All these experiments, like those of previous workers (Le Sourd and Pagniez,¹⁰⁰ Stewart and Zucker,¹⁰¹ Janeway, Richardson and Park¹⁰²), point to the platelets as the source of the muscle-stimulating substance.

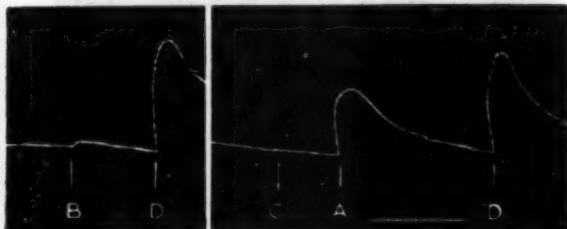


FIGURE I.

Record of the responses of a piece of ox carotid artery to serum prepared in different ways from the same sample of blood. At D, the responses are to serum prepared from freshly collected whole blood. Samples A, B and C were as follows: A, serum prepared from "gravity plasma", the cells being allowed to form a sediment by standing in the cold for twenty-four hours; B and C, serum from centrifugated plasma containing 2,000 platelets per cubic millimetre. For C the plasma was removed immediately the centrifugation was completed, while for B it was allowed to remain in contact with the sedimented cells for twenty-four hours. Time in half minutes; interval between panels five minutes.

This view was further extended by the preparation of platelet extracts. Such extracts were made in the following manner. Oxalated gravity plasma was centrifugated at 1,000 revolutions per minute for one minute, and this procedure was repeated three more times, the sediment being discarded after each centrifugation. This threw down all the formed elements other than platelets. The final supernatant fluid (platelet count, 150,000 to 200,000 per cubic millimetre) was divided, one portion being clotted by the addition of calcium chloride to provide a control serum. The other was centrifugated at 4,500 revolutions per minute for fifteen minutes, the platelet sediment being washed three times with saline solution and extracted by grinding with powdered quartz. The activity of such platelet extracts was quantitatively equal to or greater than serum made from the original platelet-containing plasma.

Evidently the active substance is preformed in the platelets, and its liberation is incidental to the clotting process. As a corollary to this observation, we were able to activate citrated platelet-rich (but not "platelet-free") plasma by mechanical shaking with glass beads for thirty to sixty minutes. In other words, citrated plasma, provided it was rich in platelets, had acquired all the muscle-stimulating and vasoconstrictor activity of serum, although the clotting process as such had never taken place.

Nature of Muscle-Stimulating and Vasoconstrictor Substances.

It was shown that serum which had been boiled still retained its muscle-stimulating and vasoconstrictor action. Ultrafiltrates through "Cellophane" membranes, which were impermeable to soluble starch but permeable to erythrodextrin, possessed all the muscle-stimulating and vasoconstrictor actions of the original serum. Serum could be freed of its activity by dialysis against distilled water through "Cellophane" membranes. These results indicate that the active substances hitherto discussed are not protein in nature.

Effects of Storage.

Serum either at room temperature or in a refrigerator at 0° to 2° C. retains its muscle-stimulating and vasoconstrictor action without appreciable reduction in activity for at least three months. This was shown by comparison of dried serum after the lapse of time with the original corresponding liquid serum.

Effects of Drying.

Drying of serum by the method of Flosdorf and Mudd is without effect on its activity. Indeed, it has already been stated that such serum was used as a standard. Serum protein prepared by the method of Hardy and Gardner is when reconstituted quite inactive.

Figure II shows at S the type of response given by the isolated jejunum of the guinea-pig to a one cubic centimetre dose of serum from whole blood, and illustrates the inactivity of reconstituted "Hardyized" serum (H₁ and H₂). The samples of serum were left in contact for thirty seconds.

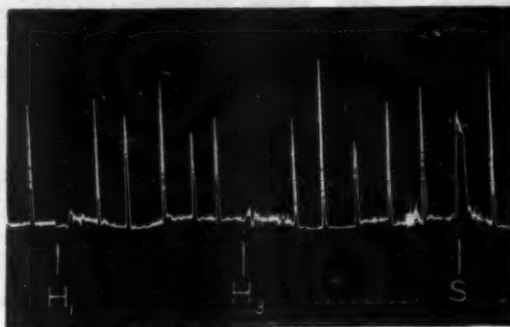


FIGURE II.

The response of an isolated strip of jejunum of the guinea-pig, to one cubic centimetre doses of two different samples of reconstituted "Hardyized" serum prepared from whole blood at H₁ and H₂ and to a one cubic centimetre dose of a standard serum prepared from whole blood at S. The unlettered responses are to doses of 0.17 of histamine. Time in half minutes.

The Alleged Presence of Adenyl Compounds in Serum.

Zipf, in 1931, showed that fresh defibrinated blood or serum contained large quantities of adenyl compounds, which he considered to be responsible for the toxicity of such fluids. These compounds are vasodilator in action and in large doses produce heart block in the intact animal. It is important, then, to determine whether any such substances are present in the serum being prepared for human transfusions.

The method which we used was sufficiently sensitive to detect 1% of adenosine per cubic centimetre of serum—an amount very much less than the quantities described by Zipf. No adenyl compounds could be detected in samples of serum varying in age from twelve hours to several weeks. This was not surprising, because we confirmed the observation of Drury, Lutwak-Mann and Solandt⁽¹⁷⁾ that serum regularly contains an enzyme which inactivates adenosine added to the serum. The findings of Zipf⁽¹⁸⁾ and Fiske⁽¹⁹⁾ must be attributable to the fact that they used very fresh defibrinated blood or serum.

The Effect of Serum Injections in the Cat, Dog and Rabbit.

Recently Buttle *et alii*⁽²⁰⁾ have described unsatisfactory results following the experimental transfusion of cat serum into cats suffering from hæmorrhage. Brodie,⁽²¹⁾ in 1900, using the same animal, described a fall of blood pressure and respiratory disturbances following the intravenous injection of both cat and foreign serum, but not of plasma. In view of these results we have reinvestigated the nature of this phenomenon, which we have called the Brodie effect, and have determined the constituent of serum which is responsible for it.

The intravenous injection of homologous serum made from whole blood in doses of one to ten cubic centimetres produces in the cat, but not in the dog or rabbit, a profound fall in the systemic blood pressure, which appears within one minute after the injection and lasts usually for two to five minutes. The fall is sometimes more prolonged and is occasionally either at an early or late stage terminated by death. The effect occurs even when serum is given to the cat which had originally provided it some twenty-four

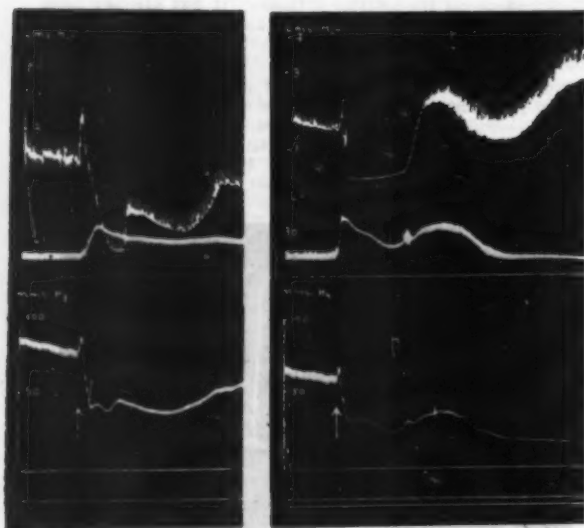


FIGURE III.

Record of the pulmonary venous (upper), pulmonary arterial (middle), and carotid arterial (lower) blood pressures from two different cats weighing 2.6 and 2.9 kilograms respectively. At the arrows 5 cubic centimetres of cat serum prepared from whole blood were injected. The pressures returned to the original levels in the case of the first cat eight minutes after injection. The experiment on the second cat was terminated by cardiac failure. Time in half minutes.

hours or more previously. The fall of systemic blood pressure still occurs after division of the vagi or atropinization or decapitation and pithing, and is associated with a sharp rise in the pressure in the pulmonary artery and a fall in the pressure in the pulmonary vein. Occasionally the rise in pressure in the pulmonary artery is interrupted or terminated by cardiac failure. Figure III illustrates these effects in the cat and Figure IV shows their absence in the rabbit.

In experiments with the isolated cat's heart perfused with Ringer's solution, the injection of one to five cubic centimetres of serum proximal to the aortic cannula produced slight coronary vasoconstriction lasting one or two minutes. Otherwise the effect of serum was dynamic, the heart rate and the amplitude of the beats increasing for about five minutes. There was no direct vasodilator action on the mesentery.

As a result of these observations we concluded that the fall of the systemic blood pressure in the cat was due mainly to pulmonary vasoconstriction, coronary constriction possibly playing a small part.

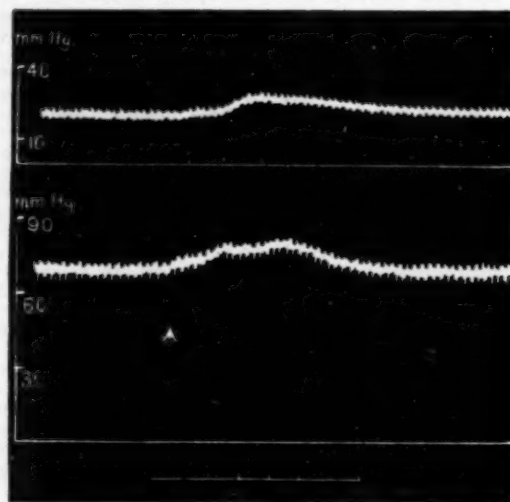


FIGURE IV.

Record of the blood pressures in the pulmonary (upper) and carotid (lower) arteries from a rabbit weighing 2.0 kilograms. At the arrow 10 cubic centimetres of serum were injected intravenously. Time in half minutes.

Nature of Active Substance in Serum Producing the Brodie Effect.

Cat serum prepared from platelet-free plasma is without activity on the cat's blood pressure, whereas serum prepared from platelet-rich plasma produces the usual effect. Extracts of platelets in saline solution, provided they have not been boiled, also produce the Brodie effect. Nevertheless, this phenomenon in the cat is not due to the vasoconstrictor substance already described, which is derived from the blood platelets, because there is no constant parallelism between the effects of different specimens of serum on the ox carotid on the one hand and on the cat's blood pressure on the other. Moreover, the active principle which produces the Brodie effect, unlike the vasoconstrictor substance derived from the platelets, is destroyed by boiling, is not dialysable and cannot be obtained in an ultrafiltrate. Human serum prepared from whole blood produces similar effects in the cat, but the difference in effect between it and plasma or between it and serum prepared from centrifuged plasma is not regularly obtained. This is because a number of foreign proteins (for example, egg albumen—Brodie⁽²²⁾) may produce the Brodie effect as well as a heat-labile, non-dialysable (probably protein-like) substance which is liberated into serum from platelets in the clotting process. This substance is responsible for all the activity of homologous serum in producing a fall in the systemic blood pressure of the cat.

Relationship of these Observations to Serum Transfusions in Man.

Conclusions as to the importance or otherwise of these pharmacological properties of serum must be based ultimately on clinical experience. Inferences drawn from experiments such as those of Buttle *et alii*,⁽²⁰⁾ in which

serum was given to cats in the treatment of experimental hemorrhage, are probably misleading. These observers bled cats of 50% of their blood volume and immediately transfused them with various substitutes, including whole blood, plasma, serum, gum saline solution, hemoglobin saline solution. They concluded that plasma was the only substitute whose value consistently approximated to that of whole blood. Serum produced respiratory disturbances and severe vascular reactions at the beginning of transfusion, causing the death of some animals. The conclusion of Buttle *et alii* was not at all surprising, for the results described above, like those of Brodie in 1900, indicate that the cat, but not the dog or rabbit, reacts to its own serum in a very special manner. So pronounced sometimes is this reaction after very small doses of serum that if there were any evidence that man behaved in an analogous fashion the intravenous use of human serum would certainly be out of the question. There is, in fact, no evidence that man does behave in such a manner to injections of human serum. It is significant also that Maglader, Solandt and Best¹⁰ and others¹¹ who worked with dogs concluded that serum was a very satisfactory blood substitute.

So far, in this discussion the term serum has been used without qualification as to its mode of preparation. In the animal experiments of Buttle, of Brodie, and of Maglader, Solandt and Best, it was prepared from whole blood. Our results, however, have indicated that, according to its mode of preparation, serum may vary greatly in its content of pharmacologically active substances and that there exist relatively simple methods of preparing human serum which shall contain pharmacologically active substances in minimal amounts. These methods depend in principle on the preparation of serum by the recalcification of plasma which has been centrifugated or "cream separated" in order to free it from all or from a large proportion of its platelets. At present, in this country serum is being prepared from centrifugated plasma at the Commonwealth Serum Laboratories and from "cream-separated" plasma in both Melbourne and Sydney. "Cream-separated" plasma has a higher platelet count than plasma centrifugated at high speed; but the serum it yields on clotting has only about one-fourth or one-third of the activity of that prepared from whole blood. Both of these methods have the additional advantage that they give a higher yield of serum than the method of merely allowing whole blood to clot. In addition, reconstituted "Hardyized" serum protein, as regards muscle stimulation and vasoconstrictor action, is inactive.

So far as clinical experience is concerned, it is difficult to assess reports on the inferiority of serum in relation to the pharmacologically active substances which may be present, because so many reports do not make it clear how the serum was prepared. Apart from this, sometimes the serum was filtered, sometimes unfiltered; sometimes no statement is made on the matter. Moreover, in some of the reports on the inferiority of serum, one finds (i) that insufficient cases were observed (Black¹²), (ii) that concentrated serum was used (Aldrich *et alii*,¹³ Black,¹⁴ Brown and Mollison,¹⁵ or (iii) that the possibility of pyrogens could not be excluded. It is perhaps significant that the reactions described as following the use of serum have been mainly febrile and do not differ in type from the reactions sometimes occurring with plasma or whole blood (fresh or stored). It is difficult to see how the muscle-stimulating substances can be responsible for such reactions. In point of fact, however, numerous reports (Bond and Wright,¹⁶ Wright *et alii*,¹⁷ Clegg and Dible,¹⁸ Hill *et alii*,¹⁹ Bick and Drevermann,²⁰ and others) indicate that serum is quite safe. In these reports serum was prepared from whole blood in some cases and from centrifugated plasma in others. There is thus no evidence that these pharmacological properties are responsible for serum reactions, though it is theoretically possible that they may be important in producing circulatory reactions when one is concerned with a very large dose in a susceptible subject.

In view of the fact that serum possesses certain practical advantages over plasma from the point of view of preparation, it is important to emphasize that there is no real clinical evidence that properly prepared serum is in any

way inferior to plasma as a blood substitute. Moreover, the theoretical objection to the presence of pharmacologically active substances in serum may be avoided if it is prepared from centrifugated or "cream-separated" plasma, or if reconstituted "Hardyized" serum protein is used.

Summary.

1. In the process of blood clotting there occurs (incidental to the clotting process) a liberation of a smooth muscle stimulating and vasoconstrictor substance into the serum. This substance is liberated from the blood platelets; it withstands boiling and is ultrafilterable. The activity of serum is maximal when it is made from clotted whole blood and minimal when it is made from centrifugated plasma. Serum retains its activity with little or no diminution for at least three months.

2. Adenyl compounds are not present in human serum twelve hours or more after preparation. Serum contains an enzyme which inactivates adenosine.

3. The cat (but not the dog or rabbit) reacts to the administration of homologous serum by pulmonary vasoconstriction resulting in a sharp fall of systemic blood pressure. The serum constituent responsible for this is protein in nature and derived from platelets. Proteins foreign to the animal concerned may produce the effect also.

4. Conclusions as to the importance of these properties so far as transfusions in man are concerned must be based on clinical experience. There is so far no evidence to suggest that serum properly prepared from either blood or plasma is unsafe. However, it is preferable to prepare serum from "platelet-free" plasma produced either by centrifugation or in a cream separator. These methods, as well as giving a greater yield of serum, ensure that pharmacologically active substances which are derived from the platelets shall be present in minimal amounts. Reconstituted "Hardyized" serum protein is also pharmacologically inactive.

Acknowledgements.

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The method which we used was sufficiently sensitive to detect 1% of adenosine per cubic centimetre of serum—an amount very much less than the quantities described by Zipf. No adeny compounds could be detected in samples of serum varying in age from twelve hours to several weeks. This was not surprising, because we confirmed the observation of Drury, Lutwak-Mann and Solandt⁽¹⁷⁾ that serum regularly contains an enzyme which inactivates adenosine added to the serum. The findings of Zipf⁽¹⁸⁾ and Fiske⁽¹⁹⁾ must be attributable to the fact that they used very fresh defibrinated blood or serum.

The Effect of Serum Injections in the Cat, Dog and Rabbit.

Recently Buttle *et alii*⁽²⁰⁾ have described unsatisfactory results following the experimental transfusion of cat serum into cats suffering from hemorrhage. Brodie⁽²¹⁾ in 1900, using the same animal, described a fall of blood pressure and respiratory disturbances following the intravenous injection of both cat and foreign serum, but not of plasma. In view of these results we have reinvestigated the nature of this phenomenon, which we have called the Brodie effect, and have determined the constituent of serum which is responsible for it.

The intravenous injection of homologous serum made from whole blood in doses of one to ten cubic centimetres produces in the cat, but not in the dog or rabbit, a profound fall in the systemic blood pressure, which appears within one minute after the injection and lasts usually for two to five minutes. The fall is sometimes more prolonged and is occasionally either at an early or late stage terminated by death. The effect occurs even when serum is given to the cat which had originally provided it some twenty-four

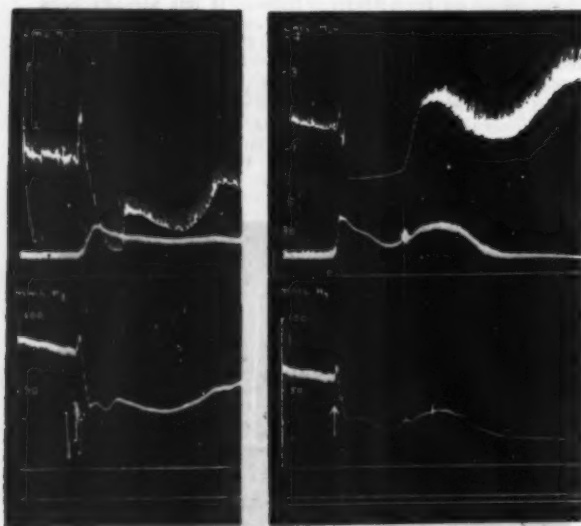


FIGURE III.

Record of the pulmonary venous (upper), pulmonary arterial (middle), and carotid arterial (lower) blood pressures from two different cats weighing 2.6 and 2.9 kilograms respectively. At the arrows 5 cubic centimetres of cat serum prepared from whole blood were injected. The pressures returned to the original levels in the case of the first cat eight minutes after injection. The experiment on the second cat was terminated by cardiac failure. Time in half minutes.

hours or more previously. The fall of systemic blood pressure still occurs after division of the vagi or atropinization or decapitation and pithing, and is associated with a sharp rise in the pressure in the pulmonary artery and a fall in the pressure in the pulmonary vein. Occasionally the rise in pressure in the pulmonary artery is interrupted or terminated by cardiac failure. Figure III illustrates these effects in the cat and Figure IV shows their absence in the rabbit.

In experiments with the isolated cat's heart perfused with Ringer's solution, the injection of one to five cubic centimetres of serum proximal to the aortic cannula produced slight coronary vasoconstriction lasting one or two minutes. Otherwise the effect of serum was dynamic, the heart rate and the amplitude of the beats increasing for about five minutes. There was no direct vasodilator action on the mesentery.

As a result of these observations we concluded that the fall of the systemic blood pressure in the cat was due mainly to pulmonary vasoconstriction, coronary constriction possibly playing a small part.

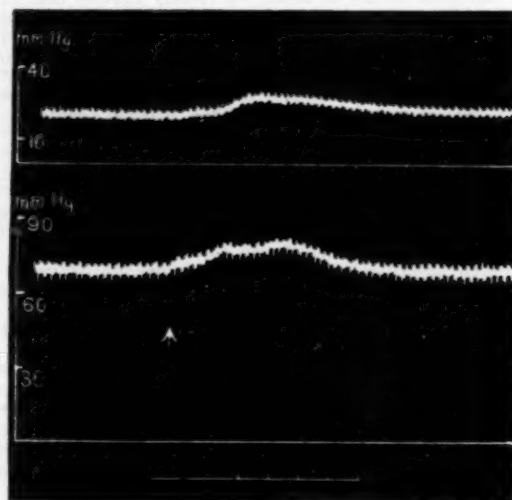


FIGURE IV.

Record of the blood pressures in the pulmonary (upper) and carotid (lower) arteries from a rabbit weighing 2.6 kilograms. At the arrow 10 cubic centimetres of serum were injected intravenously. Time in half minutes.

Nature of Active Substance in Serum Producing the Brodie Effect.

Cat serum prepared from platelet-free plasma is without activity on the cat's blood pressure, whereas serum prepared from platelet-rich plasma produces the usual effect. Extracts of platelets in saline solution, provided they have not been boiled, also produce the Brodie effect. Nevertheless, this phenomenon in the cat is not due to the vasoconstrictor substance already described, which is derived from the blood platelets, because there is no constant parallelism between the effects of different specimens of serum on the ox carotid on the one hand and on the cat's blood pressure on the other. Moreover, the active principle which produces the Brodie effect, unlike the vasoconstrictor substance derived from the platelets, is destroyed by boiling, is not dialysable and cannot be obtained in an ultrafiltrate. Human serum prepared from whole blood produces similar effects in the cat, but the difference in effect between it and plasma or between it and serum prepared from centrifugated plasma is not regularly obtained. This is because a number of foreign proteins (for example, egg albumen—Brodie⁽²²⁾) may produce the Brodie effect as well as a heat-labile, non-dialysable (probably protein-like) substance which is liberated into serum from platelets in the clotting process. This substance is responsible for all the activity of homologous serum in producing a fall in the systemic blood pressure of the cat.

Relationship of these Observations to Serum Transfusions in Man.

Conclusions as to the importance or otherwise of these pharmacological properties of serum must be based ultimately on clinical experience. Inferences drawn from experiments such as those of Buttle *et alii*,⁽²⁰⁾ in which

serum was given to cats in the treatment of experimental hemorrhage, are probably misleading. These observers bled cats of 50% of their blood volume and immediately transfused them with various substitutes, including whole blood, plasma, serum, gum saline solution, hemoglobin saline solution. They concluded that plasma was the only substitute whose value consistently approximated to that of whole blood. Serum produced respiratory disturbances and severe vascular reactions at the beginning of transfusion, causing the death of some animals. The conclusion of Buttle *et alii* was not at all surprising, for the results described above, like those of Brodie in 1900, indicate that the cat, but not the dog or rabbit, reacts to its own serum in a very special manner. So pronounced sometimes is this reaction after very small doses of serum that if there were any evidence that man behaved in an analogous fashion the intravenous use of human serum would certainly be out of the question. There is, in fact, no evidence that man does behave in such a manner to injections of human serum. It is significant also that Maglader, Solandt and Best⁽³⁾ and others⁽⁴⁾ who worked with dogs concluded that serum was a very satisfactory blood substitute.

So far, in this discussion the term serum has been used without qualification as to its mode of preparation. In the animal experiments of Buttle, of Brodie, and of Maglader, Solandt and Best, it was prepared from whole blood. Our results, however, have indicated that, according to its mode of preparation, serum may vary greatly in its content of pharmacologically active substances and that there exist relatively simple methods of preparing human serum which shall contain pharmacologically active substances in minimal amounts. These methods depend in principle on the preparation of serum by the recalcification of plasma which has been centrifugated or "cream separated" in order to free it from all or from a large proportion of its platelets. At present, in this country serum is being prepared from centrifugated plasma at the Commonwealth Serum Laboratories and from "cream-separated" plasma in both Melbourne and Sydney. "Cream-separated" plasma has a higher platelet count than plasma centrifugated at high speed; but the serum it yields on clotting has only about one-fourth or one-third of the activity of that prepared from whole blood. Both of these methods have the additional advantage that they give a higher yield of serum than the method of merely allowing whole blood to clot. In addition, reconstituted "Hardyized" serum protein, as regards muscle stimulation and vasoconstrictor action, is inactive.

So far as clinical experience is concerned, it is difficult to assess reports on the inferiority of serum in relation to the pharmacologically active substances which may be present, because so many reports do not make it clear how the serum was prepared. Apart from this, sometimes the serum was filtered, sometimes unfiltered; sometimes no statement is made on the matter. Moreover, in some of the reports on the inferiority of serum, one finds (i) that insufficient cases were observed (Black⁽⁵⁾), (ii) that concentrated serum was used (Aldrich *et alii*,⁽⁶⁾ Black,⁽⁷⁾ Brown and Mollison,⁽⁸⁾ or (iii) that the possibility of pyrogens could not be excluded. It is perhaps significant that the reactions described as following the use of serum have been mainly febrile and do not differ in type from the reactions sometimes occurring with plasma or whole blood (fresh or stored). It is difficult to see how the muscle-stimulating substances can be responsible for such reactions. In point of fact, however, numerous reports (Bond and Wright,⁽⁹⁾ Wright *et alii*,⁽¹⁰⁾ Clegg and Dible,⁽¹¹⁾ Hill *et alii*,⁽¹²⁾ Bick and Drevermann,⁽¹³⁾ and others) indicate that serum is quite safe. In these reports serum was prepared from whole blood in some cases and from centrifugated plasma in others. There is thus no evidence that these pharmacological properties are responsible for serum reactions, though it is theoretically possible that they may be important in producing circulatory reactions when one is concerned with a very large dose in a susceptible subject.

In view of the fact that serum possesses certain practical advantages over plasma from the point of view of preparation, it is important to emphasize that there is no real clinical evidence that properly prepared serum is in any

way inferior to plasma as a blood substitute. Moreover, the theoretical objection to the presence of pharmacologically active substances in serum may be avoided if it is prepared from centrifugated or "cream-separated" plasma, or if reconstituted "Hardyized" serum protein is used.

Summary.

1. In the process of blood clotting there occurs (incidental to the clotting process) a liberation of a smooth muscle stimulating and vasoconstrictor substance into the serum. This substance is liberated from the blood platelets; it withstands boiling and is ultra-filterable. The activity of serum is maximal when it is made from clotted whole blood and minimal when it is made from centrifugated plasma. Serum retains its activity with little or no diminution for at least three months.

2. Adenyl compounds are not present in human serum twelve hours or more after preparation. Serum contains an enzyme which inactivates adenosine.

3. The cat (but not the dog or rabbit) reacts to the administration of homologous serum by pulmonary vasoconstriction resulting in a sharp fall of systemic blood pressure. The serum constituent responsible for this is protein in nature and derived from platelets. Proteins foreign to the animal concerned may produce the effect also.

4. Conclusions as to the importance of these properties so far as transfusions in man are concerned must be based on clinical experience. There is so far no evidence to suggest that serum properly prepared from either blood or plasma is unsafe. However, it is preferable to prepare serum from "platelet-free" plasma produced either by centrifugation or in a cream separator. These methods, as well as giving a greater yield of serum, ensure that pharmacologically active substances which are derived from the platelets shall be present in minimal amounts. Reconstituted "Hardyized" serum protein is also pharmacologically inactive.

Acknowledgements.

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TRAUMATIC SHOCK AND CONCUSSION.

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SHOCK.

The term "shock" was originally used by James Latta, of Edinburgh, in 1795, to describe the state of collapse of the circulation following severe injury (Kinnaman, 1903). Arterial blood pressure depends upon three factors: (i) the force of the heart beat, (ii) the peripheral resistance, and (iii) the volume and viscosity of the blood. Any condition, therefore, which interferes adversely with any one of these will, if of sufficient severity, produce a fall in blood pressure, accompanied by collapse of the circulation.

The force of the heart beat depends primarily upon the venous inflow—that is, the amount of blood entering the heart in diastole—since the greater the distension of the heart muscle fibres by filling, the more forcible will be their contraction. The force of the heart beat may

therefore be lessened by diminished venous inflow. It may also be lessened by lowered arterial resistance; by reflex vagal inhibition of the heart itself (syncope); by anatomical defects of the heart, congenital or acquired; and by degeneration or inflammation of the myocardium from infection or toxæmia, acute or chronic. When the systolic blood pressure falls to 80 millimetres of mercury cardiac contraction begins to weaken. When the systolic blood pressure falls to 75 millimetres of mercury the secretion of urine ceases (Winton, 1937). When the systolic blood pressure falls to 60 millimetres of mercury complete collapse of the circulation occurs, and if this is allowed to persist for half an hour it is likely to bring about permanent changes, which may be fatal. In such a state of collapse, heat production is reduced by more than 50% (National Health Insurance Medical Research Committee, Special Report Series Numbers 25 and 26).

The peripheral resistance may be lowered by dilatation of the peripheral arteries and capillaries through vasomotor action, and by dilatation of and damage to the capillaries through circulation in the blood of drugs, chemicals and toxins—such as carbon dioxide, lactic acid, histamine and bichloride of mercury—which cause stasis with subsequent exudation and loss of plasma.

The volume of the blood may be reduced by hæmorrhage; by loss of fluid, as in cholera, excessive diuresis, sweating or vomiting; by diminished fluid intake; and by exudation of plasma in prolonged capillary stasis. The viscosity of the blood may be diminished by increased intake of fluid, either orally or parenterally, and conversely may be increased by diminished intake of fluid and by excessive loss of fluid or exudation of plasma in the conditions enumerated above. With a blood volume of below 80% the patient shows serious symptoms of collapse, while if the blood volume is below 65% his condition is critical (National Health Insurance Medical Research Committee, Special Report Series Number 26).

In shock, four vital processes are notably depressed: the temperature is subnormal, the blood pressure falls very low, the pulse is extremely feeble, running and irregular, and the respirations are shallow and sighing (Boyd, 1933). The symptoms as described by Rose and Carless (1937) vary from slight momentary giddiness or faintness to complete prostration, insensibility and even death.

In a case of shock of moderate severity the patient lies in a state of apathetic torpor, from which he is aroused with difficulty; but if so aroused, he can answer intelligently, though faintly. The surface of the body is cold and pallid, and often covered with a cold, clammy sweat; the pupils are dilated; the temperature is subnormal and gradually falls; the pulse is weak, running and perhaps uncountably quick; the eyes are sunken; the finger-tips, the lips, and the extremities of the nose and ears gradually become blue and livid; the secretion of urine is diminished; the respirations are rapid and shallow, becoming irregular; the mouth is parched, the sugar content of the blood is raised, and the patient complains of intense thirst. Gradually he passes into a state of complete unconsciousness and dies of respiratory failure.

Clinical observation has shown that the degree of shock depends on the nature of the injury and on the number of sensory nerves involved. Thus trauma to organs with a rich sensory supply, such as the testis, intestine or hand, will produce much shock; an extensive laceration of the skin will be more productive of shock than a deep cut, and a superficial burn of the first or second degree involving half the body surface is more dangerous than the complete incineration of a hand.

The post-mortem features of traumatic shock are thus reported by O'Shaughnessy and Slome (1935):

The characteristic feature after death from traumatic shock is general pallor of the viscera, especially of the intestines and the omentum. The liver and kidneys do not bleed readily when cut. Oedema of the pancreas is never observed. The spleen is contracted, but red in colour. The lungs are generally pale. The heart contains little blood. Frequently the left ventricle is in a state of tonic contraction.

The physiological changes which accompany collapse of the circulation are described by Dale, Laidlaw, and

Richards (1919), with special reference to the injection of histamine into a cat. Histamine is derived from the amino-acid histidine, by the removal of carbon dioxide. It has an intensely stimulating action on plain muscle, including that of the arteries. When injected intravenously in large doses into laboratory animals it causes typical shock-like collapse of the circulation, accompanied by arterial constriction, diminished blood volume, concentration of the blood and failure of cardiac output. Intravenous injection of histamine dilates all the capillaries of the body, whereas stimulation of the sympathetic nervous system or perfusion with adrenaline dilates the muscle capillaries only (Halliburton and McDowall, 1937).

According to Dale, Laidlaw and Richards (1919), if the chest of such a laboratory animal is opened while continued artificial respiration is maintained, the following observations can be made:

It is seen that the heart is indeed beating strongly and regularly, but that its chambers contain remarkably little blood. Compression of the ventricles between the fingers causes scarcely a movement of the mercury in the arterial manometer. The *venae cavae* in the thorax are seen to be flaccid and half empty, and when the abdomen is opened it is seen that the abdominal cava is poorly filled with blood, while the portal vein is flat and almost empty. The arteries, both large and small, similarly contain but little blood and appear to be constricted rather than dilated. The liver is moderately pale and certainly not distended with blood, and the same is true of the spleen.

The blood, then, is not in the heart, arteries or large veins, and no large part of it is accumulated in liver and spleen. What has become of the missing volume, which normally circulates rapidly filling the heart and great vessels?

A process of exclusion led us inevitably to the capillaries in attempting to locate the lost blood... Direct inspection of the internal organs, so far as it gave information, tended to confirm this view. The arterioles supplying blood to the bowel, down to their finest microscopic branchings, contain but little blood, but the bowel itself shows a diffuse, dusky congestion, and the smallest venules are rendered visible on its surface by their content of dark blood. In the skeletal muscles mere visual examination usually gives little information; but it is certain that a similar accumulation and partial stagnation must occur in them, since the shock (i.e. collapse) can be produced with all its typical features after complete removal of the abdominal viscera. Moreover, if the volume of blood in the animal is increased by transfusion before the shock (i.e. collapse) is produced, the accumulation in the capillaries of the skeletal muscles during the shock (i.e. collapse) becomes very obvious.

McDowall (1933) writes on the same subject:

As a result of capillary dilatation there is a relative insufficiency of blood, the animal as it were bleeding into its own capillaries which have become opened up. The state is like one of hemorrhage, only the animal bleeds into its own vessels, but the capillaries are not necessarily congested, for on becoming dilated they apparently become more permeable and the blood plasma passes out into the tissues leaving behind a concentrated blood.

The finding of a concentrated blood clinically is strongly suggestive that the case is one due to capillary dilatation.

In 1927 McDowall made the following statements:

Many of the mechanisms by which the body attempts to compensate for hemorrhage depend on the carriage of afferent impulses to the vasomotor centres which in turn send out impulses to constrict the spleen and blood vessels generally.

The pressor influence of the vasomotor centre extends not only to the arteries, but also to the veins and capillaries whose capacity is reduced thereby.

It is particularly to be noted that owing to this generalized constriction of the vascular system, no fall may occur in blood pressure, either in shock or in hemorrhage, until blood volume has diminished to a considerable degree. Regarding the fall in blood volume in shock, Cronin (1941) writes as follows:

This fall [accompanied by haemoconcentration] precedes by many hours the fall in blood pressure. The latter is a comparatively late effect of shock, and [blood pressure] may still be high when [the state of] shock is well-nigh mortal.

Freeman *et alii* (1936) report that the blood flow through the hand in clinical cases of surgical shock is much reduced and that the low oxygen saturation of the

venous blood is an indication of the severity of the tissue asphyxiation.

Sampson Wright (1936), in referring to the generalized capillary dilatation produced by histamine, states that in histamine poisoning the intestines, pancreas and other solid viscera are intensely congested and tend to become oedematous.

The post-mortem appearances of the viscera in histamine poisoning are therefore altogether different from those in shock. In the former the viscera are intensely congested, whereas in shock they are pale and anæmic.

Adrenaline.

All changes known to occur in shock can be reproduced by prolonged stimulation of the sympathetic nervous system with adrenaline. Adrenaline is the active principle of the medulla of the adrenal gland, which is developed from that part of the neural crest which subsequently becomes differentiated into the sympathetic and posterior root ganglia. The intravenous injection of adrenaline has the same effects as stimulation of the sympathetic nervous system, or stimulation of a sensory nerve (pain). The secretion of adrenaline is excited by asphyxia, by emotion and by stimulation of the splanchnic nerves.

In 1919 Erlanger and Gasser perfused adrenaline for periods of twenty to thirty minutes into a laboratory animal at such a rate as to cause high arterial pressure. When sufficiently large doses were given, the blood pressure subsequently fell steadily until the animal succumbed, though vasoconstriction persisted. They concluded that a reduced blood volume, either real or effective, was the main factor at fault, and found that the post-mortem appearances were similar to those found in shock. They stated that apathy as well as other signs of shock were present in the living animal.

Freeman (1933) perfused adrenaline in physiological amounts into dogs for two hours. In his experiments he noted an immediate rise, and later a gradual fall, of blood pressure. There was a decrease in the total blood volume of 8.5% to 27%, with a relatively greater decrease in plasma volume—the same state of affairs as that found in shock. This change in the blood was prevented by a preliminary dose of ergotoxine, which paralyses the sympathetic nervous system.

From these, as well as from the earlier experiments of Erlanger and Gasser referred to above, Freeman concluded that shock was due to loss of blood volume following persistent vasoconstriction through hyperactivity of the sympathetic nervous system.

Freeman writes:

If we examine all factors which are at present known to produce shock or to aggravate the condition if present, we find that they have one physiological action in common: they are all adequate stimuli for producing hyperactivity of the sympathetic nervous system.

Stimuli, such as those caused by traction on the mesentery or parietal portion of the peritoneum, or stimulation of a sensory nerve, produce a rise in blood pressure, owing to constriction of the cutaneous and splanchnic blood vessels, which is followed by a fall when the stimulus ceases. If these stimuli are continued, after a certain time, which depends on the nature and number of stimuli, the mean blood pressure gradually falls, the blood concentration increases, and the rises in pressure from stimulation become less and less, until the animal succumbs of respiratory failure—a sequence of events similar to that produced by the perfusion of an animal with adrenaline.

Elsewhere I have suggested (Tomb, 1937) that most of the confusion regarding the true nature of shock has arisen from failure to appreciate the fact that stimulation of the sympathetic nervous system results in the dilatation of the capillaries of the skeletal muscles, as well as in the constriction of those of the skin and abdomen. When, therefore, the sympathetic nervous system is stimulated, the rise or fall in blood pressure at any moment will depend upon the balance of forces between the fall of pressure produced by dilatation of the capillaries of the

skeletal muscles, and the rise of pressure produced by constriction of those of the skin and abdomen. This balance of forces is well seen in the action of adrenaline on the volume of the limb of a laboratory animal. Adrenaline is a stimulator of the sympathetic nervous system, and as such it constricts the cutaneous blood vessels while dilating those of the muscles. If the intact limb of such an animal is measured by plethysmograph, it is found to diminish in volume after the injection of adrenaline owing to the dominating effect of the constriction of the cutaneous blood vessels; but if the limb is now skinned, its volume is found to increase, owing to the unopposed dilatation of the muscle blood vessels.¹

The suggestion referred to above has received the authoritative support of McDowall (1940), who writes as follows:

It is not, however, so well known that adrenaline causes a dilatation of the vessels of the muscles. We have become obsessed by the classical picture of the rise of the blood pressure resulting from the injection of an enormous dose of adrenaline, a dose many times that ever secreted. It can easily be shown that minute doses of adrenaline, quite insufficient to raise the blood pressure, dilate the vessels of the muscles at the same time as they constrict the vessels of the skin . . .

The possibility that the sympathetic-adrenal system may be overstimulated [in shock] now receives most serious consideration . . . The possibility is based on the work of Freeman, who showed that if adrenaline is infused into an animal at the rate it is normally secreted the animal passes into a state of shock associated with a concentration of blood and low blood volume . . .

Freeman suggests that in the production of shock the sympathetic by its [over]-activity causes intense vasoconstriction, a peripheral asphyxia and capillary dilatation, and thus sets up the vicious circle. . . . I am, however, inclined to think that the driving of the blood into the relaxed vessels of the muscles may be just as important and allow loss of blood plasma . . . It is of special interest to remark that Freeman has found that shock is prevented . . . by removal of the sympathetic or its paralysis by ergotoxine.

The Sympathetic Nervous System.

The sympathetic nervous system is dependent on the central nervous system and is controlled by ganglia situated in the lower part of the wall of the third ventricle and upper part of the iter. According to Halliburton and McDowall (1937), it may be looked upon as adapting the body to the needs of muscular activity, emotion and exposure to cold.

Its most important functions are to increase the heart rate, to maintain blood pressure and to mobilize glucose. It constricts the cutaneous and splanchnic blood vessels (which constitute the great blood reservoirs of the body) and dilates the blood vessels of the skeletal muscles. It also dilates the pupil and causes the secretion of sweat.

Stimulation of the sympathetic nervous system therefore produces a train of effects identical with the symptoms recorded above as associated with traumatic shock. (i) The sugar content of the blood is raised. (ii) The cutaneous and splanchnic blood vessels are constricted; which accounts for the chilliness and pallor and (in many instances) for a primary rise in blood pressure. (iii) The blood vessels and capillaries of the skeletal muscles are dilated; which accounts for the accompanying fall of blood pressure and ultimate collapse. (iv) The pupils are dilated. (v) The secretion of sweat is increased.

Most of the activities of the sympathetic nervous system are also brought about by the injection of adrenaline into the blood stream and by the accumulation of carbon dioxide in the body. The apparent object of this mechanism is to make available for the active muscles a maximum amount of oxygen-carrying blood, at the temporary expense of those parts of the body whose activity is not immediately required—for example, the skin and abdominal organs. The sympathetic makes it possible for the body to use its accumulated stores of potential energy without having recourse to its immediate environ-

ment for anything but oxygen, which it cannot store to any appreciable extent, but which is always available in the normal atmosphere.

The sympathetic nervous system is constantly receiving impulses from all parts of the body, through afferent nerves, both somatic and sympathetic, and transmitting corresponding ("sympathetic") efferent impulses through the white *rami communicantes* to the organs and structures innervated by it. Where the reception of afferent impulses is blocked (as in spinal anaesthesia) the transmission of efferent impulses, we find, is correspondingly reduced. In sleep or during chloroform anaesthesia, owing to the cutting off of the flow of normal afferent impulses, blood pressure is found to fall by 20 millimetres of mercury (Gray and Parsons, 1912). In spinal anaesthesia, when more afferent impulses are cut off, the fall in blood pressure is still greater. The collapse that is likely to occur in high spinal anaesthesia is due to the fact that all afferent impulses from the abdomen and lower limbs are cut off, with resultant loss of tone of the corresponding capillaries, both cutaneous and splanchnic, owing to cessation of normal efferent constrictor impulses.

The activity of the sympathetic nervous system is specially related to sensation and to afferent impulses which may not reach consciousness. According to Halliburton and McDowall (1937), all the actions of the sympathetic are essentially reflex in nature and depend upon afferent impulses, which reach the system from the external environment or internal structures.

The stimulation of afferent nerves with the production of pain in man, or stimulation in anesthetized animals, causes sympathetic activity, which is evidenced by dilatation of the pupil, acceleration of the heart rate and contraction of the cutaneous and splanchnic blood vessels. This effect is a reflex one via the posterior root fibres, and the white *rami communicantes* of the sympathetic. Although general anaesthesia may abolish the connexion between the posterior and the anterior roots, the connexion between the posterior roots and the white *rami* of the sympathetic is unaffected.

This accounts for the fact that shock develops during many surgical operations, despite general anaesthesia. Records taken during operations under general anaesthesia show that at certain stages when sensory nerves are stimulated a pronounced fall in blood pressure occurs, and this is intensified by rough handling or tearing of the tissues (Rose and Carless, 1937). Spinal anaesthesia blocks both connexions.

Spinal Anaesthesia.

When great operative shock is anticipated, spinal anaesthesia is ideal, for it effectually blocks all the nervous paths of shock impulses (Rose and Carless, 1937). According to Evans (1929), spinal anaesthesia not only prevents further shock in operations on patients suffering from severe shock, as in severe crushing of the limbs, but actually diminishes the shock already present. This is accounted for by the fact that in traumatic shock the fall in blood pressure is due to the reception by the sympathetic nervous system of an abnormal flood of stimuli. When this over-stimulation is diminished by spinal anaesthesia blood pressure tends to return to normal. On the other hand, in the absence of shock spinal anaesthesia causes a fall in blood pressure through interference with the reception of normal stimuli.

It may here conveniently be noted that collapse from spinal anaesthesia apart from the influence of gravity is chiefly due to excessive dilatation (through loss of tone) of the corresponding cutaneous and splanchnic capillaries from under-stimulation of the sympathetic nervous system; whereas collapse in shock is due to excessive dilatation of the capillaries of the skeletal muscles (accompanied by constriction of the cutaneous and splanchnic capillaries) from over-stimulation of the sympathetic nervous system.

Regarding the alleged failure of spinal anaesthesia, in many cases, to prevent the development of surgical and

¹ The coronary vessels, like those of the skeletal muscles, are dilated by adrenaline.

traumatic shock, the following essentials were pointed out by Lockhart-Mummery (1939):

It is essential that patients under spinal anaesthesia should be kept with the head lower than the buttocks during the whole period of anaesthesia and for some time afterwards: the reason for this being that one of the results of spinal block is to allow the blood to drain into the . . . areas . . . uncontrolled by the vasomotor centre. If the patient is kept head down this drainage of the blood is prevented and the pressure is maintained in the essential parts of the circulation . . . During the world war of 1914-18 all wounded were treated on army stretchers and were kept flat, or more often with the head raised, and it was this position which caused the trouble. Spinal anaesthesia will prevent shock in badly wounded men if the patient is kept rigidly head down for some hours after the administration of the anaesthetic.

A patient under spinal anaesthesia is therefore in a state comparable to that of a "hutch" rabbit, and like it is likely to "bleed to death" into his own abdominal vessels, owing to force of gravity and the loss of splanchnic tone, if not maintained in a suitable (Trendelenburg) position for a sufficient length of time. Spinal anaesthesia, in fact, produces the state of affairs envisaged in the old (and erroneous) conception of shock, in which the bulk of the blood was assumed to stagnate in the abdominal vessels (Fischer, 1870; Wallace, Fraser and Drummond, 1917).

Morphine.

With regard to the use of morphine as a preventive of traumatic shock, Thomas and Kelly (1924) point out that Crile advocates the repeated use of morphine until the respiratory rate falls to ten to twelve per minute. They add, however, that morphine should not be used when cyanosis is present, and that it is sufficient to give it in such doses that pain and restlessness are overcome.

It is insufficiently realized that until pain has first been completely overcome it is impossible to lower the respiratory rate to a dangerous level or to produce cyanosis, using morphine in repeated doses of a quarter or a third of a grain (Tomb, 1939; Wakeley, 1940).

The role of morphine in shock is well expressed by Cronin (1941) who writes:

In the first period of shock, morphia, even in large doses, by relieving pain and anxiety will help to improve the patient's condition. In the later stages it is . . . unsound, for by depressing the respiratory centre it increases the oxygen-deficiency of the capillaries and hence their permeability.

The Capillaries.

The capillaries of the body are minute cylindrical vessels, the walls of which are composed of a single layer of elongated, flattened, nucleated, endothelial cells.

The total number of capillaries in the body is enormous. If all the capillaries in the skeletal muscles alone were open simultaneously, their volume capacity would be sufficient to contain the entire blood of the body (Krogh, 1929). According to Halliburton and McDowall (1937), some capillaries remain permanently open, while others open and close at intervals.

These changes take place independently of the arteries and veins, and depend on the oxygen requirements of the tissue supplied. The opening-up occurs in all tissues during activity, or after the cutting off of the oxygen supply.

The control of the capillaries is both sympathetic and local. The capillaries of muscle are dilated locally by carbon dioxide and by lactic acid. These chemical substances take precedence over the influence of the sympathetic, for in a rabbit's ear, when the cervical sympathetic is stimulated, the constrictor effect is seen to wear off and the capillaries to become dilated as soon as tissue asphyxiation occurs from lack of oxygen.

In normal muscles carbon dioxide is produced by the combustion of glycogen; but in muscles deprived of oxygen, glycogen is converted into lactic acid.

Rendle Short (1922) states that the calibre of the arteries and the capillaries may vary independently one of the other, and that in histamine poisoning the capillaries are dilated though the arteries are contracted.

As illustrating the control of the sympathetic nervous system over the capillaries, Bayliss (1922) writes as follows:

Large volumes of blood or gum saline can be injected [intravenously], without more than a few minutes' effect, into cats in which the blood vessels have been removed from the control of the vasomotor centre by section of the spinal cord in the cervical region. The blood pressure is raised temporarily [by such injections], but by the end of seven or eight minutes it has returned to its former low level . . . The only explanation that can be suggested is that the capillaries are normally under the control of the [sympathetic] nervous system, and in the absence of this control they become distended, and thus soak up large volumes of blood.

Regarding the increased permeability of the capillaries in shock, Bayliss (1919) writes:

The second pathological state induced by prolonged low blood-pressure in the capillaries is an increase in the permeability of the blood-vessels to colloids. Their normal state is one of impermeability to colloids, so that a solution of a colloid of sufficient osmotic pressure does not leave the circulation. If this property of the capillaries is lost, there is no force to retain fluid, and both gum-saline and blood plasma escape into the tissues. The clinical index that such a state has been reached or is coming on is a progressive concentration of the blood as regards corpuscles. As long as the blood-vessels maintain their normal state, the effect of a fall in blood-pressure is to attract fluid from the tissues. This is because the osmotic pressure of the colloids remains at its normal height, while the filtration is reduced owing to the low arterial pressure. The result is a dilution of the blood, which is a favourable sign . . .

If this increased permeability has not reached too high a value or not been present for too long a time, recovery is possible . . . It is evident, then, that the state is capable of return to normal, if not too serious. The renewed supply of oxygen restores the necessary impermeability to colloids.

To enable us the better to understand the phenomenon of collapse of the circulation in shock, it may here be profitable to recall the mechanism of the blood supply to the skeletal muscles. According to Young *et alii* (1938), when a muscle is at rest only a few capillaries are open at any given moment; but at the same time there occur a continual closing of the visible capillaries and opening of others. When a muscle contracts, nearly all the capillaries open and remain open as long as the muscle is active. The number of capillaries open in a contracting muscle may be many times greater than in the same muscle at rest. Changes, they add, must take place in the entire circulatory system if enough blood is to be brought to the muscles during periods of great activity. These changes are brought about through the agency of the vasomotor centre in the brain stem. Whenever, for example, a sudden stimulus causes someone to jump and run for his life, the arterioles and capillaries in the skin and abdomen contract, with great reduction in the amount of blood flowing to those parts, while at the same time the capillaries and arterioles of the muscles dilate so that nearly all the blood in the body is forced to flow rapidly through these latter vessels. In brief, they state, when the muscles of the body are active, activity on the part of the vasomotor centre (that is, the sympathetic nervous system) results in a shunting of the major volume of blood from the skin and abdominal organs into the muscles.

According to McDowall (1941), muscular exercise, by opening up the blood vessels of the muscles, may in certain subjects produce collapse (fainting).

Samson Wright (1937) states that the net effect of injection of adrenaline into the blood stream (that is sympathetic stimulation) is "to redistribute the blood in a manner appropriate for conditions of stress: to drive it out of the splanchnic area and skin and send it mainly to the skeletal muscles and heart".

The physiological changes in the circulatory system which accompany intense muscular activity are found in exaggerated and pathological form in traumatic shock;

thus, whenever the body receives any major injury, an excessive number of stimuli from the injured area reaches the vasomotor centre, which reacts to this over-stimulation by tightly constricting the blood vessels of the skin and abdomen and dilating those of the skeletal muscles, the result of which, as a rule, is a fall of blood pressure and ultimate collapse.

The phenomena of the collapse of the circulation in shock may thus be summarized (after Muir, 1936). During shock the cutaneous and splanchnic capillaries are tightly constricted, while those of the skeletal muscles are dilated and the blood stagnates in them. Blood pressure in consequence falls. The blood vessels of the rest of the body and particularly the peripheral arteries and veins are constricted in an effort to maintain blood pressure. Abnormal permeability of the walls of the dilated capillaries then develops owing to tissue asphyxiation, and an increased amount of blood plasma passes out of the circulation into the tissues, with the result that the blood is concentrated and blood volume is diminished. The amount of blood reaching the right side of the heart thus becomes seriously reduced, and generalized tissue asphyxiation of the body cells results.

Theories Regarding Shock.

Many theories have been advanced to account for the phenomena of shock, some of which I shall now review.

Mitchell, Keen and Moorhouse, the surgeons of the American Civil War, considered that the medulla and the vagus—that is, the vasomotor centre—were chiefly concerned in initiating the conditions of shock. Agnew (1881) attributed shock to "feebleness of the heart's action and paralysis of the walls of the blood vessels". In 1870, Fischer, relying on the experiment of Goltz, who in 1863 had shown that a blow on the exposed mesentery of a frog caused a reflex inhibition of the heart and a dilatation of the blood vessels of the abdomen, formulated the theory that in shock most of the blood stagnated in the abdominal vessels, and was thus removed from the general circulation. This theory was accepted for many years, until Wallace, Fraser and Drummond (1917) pointed out that, in the course of many hundreds of abdominal operations performed during the World War upon patients suffering from traumatic shock, they had never found any evidence of primary splanchnic congestion.

In 1899 Crile formulated the theory that shock was due to exhaustion of the vasomotor centre; but this was disproved by Porter and by Seelig and Joseph, the latter of whom showed that if in a shocked rabbit blood pressure is suddenly raised by clamping the aorta, the blood greatly distends the blood vessels of the ear, the nerves of which have been previously cut, but does not distend the blood vessels of the other ear, the nerves of which are still connected with the vasomotor centre; this showed that the centre was still holding the blood vessels in effective contraction. Pike, Guthrie and Stewart showed that the vasomotor centre was more capable of withstanding anaemia than any other of the vital centres, and that its function was the last to disappear in total anaemia (National Health Insurance Medical Research Committee, Special Report Series Number 25).

Gray and Parsons (1912) found that if at the moment of death from experimental shock a stout needle were driven into the centre of the floor of the fourth ventricle, a pronounced rise in blood pressure with acceleration of the pulse was observable; this proved that the vasomotor centre was still active in the most extreme degree of collapse.

It was also repeatedly noted by surgeons in the war of 1914-1918, while operating in cases of shock, that no bleeding occurred when vessels were cut across, owing to the strong contraction of the outlying arteries (Cannon, 1919). Miller (1927), in a close study of experimental cerebral concussion in animals, found the vasomotor centre "extraordinarily resistant to violence". Experience in the World War showed that the vasomotor centre was still active in cases of established shock, since shock was observed to be constantly increased by pain, cold, fear,

anxiety and rough handling, all of which are stimuli of the sympathetic nervous system.

In 1910 and 1911 Henderson advanced the theory that loss of carbon dioxide from the body ("acapnia") was the cause of shock; but this was proved to be erroneous by many observers.

Following the work of Dale, Laidlaw and Richards (1919), referred to above, on the state of collapse produced by the intravenous injection of histamine, Cannon and Bayliss (1919) formulated a theory of traumatic toxæmia as a factor in shock, based on the hypothetical production in traumatized tissues of histamine-like substances; but Smith (1928), Parsons and Phemister (1930), and others have shown that infusion of blood from a traumatized animal into a normal animal produces no fall in blood pressure. Moreover, the histamine content of muscle is very low, and O'Shaughnessy and Slome (1935) have shown that the amount of histamine which could possibly be derived from muscle injury in experimental traumatic shock is totally inadequate to produce shock in the animal concerned; furthermore, the amount of histamine necessary to produce shock by intramuscular injection is ten times that found necessary by intravenous injection. O'Shaughnessy and Slome (1935) finally conclude that "a toxæmia due to the elaboration of histamine or any other depressor substance, manufactured in the traumatized area, plays no part in the syndrome of traumatic shock". They are of the opinion that it is the continuance of abnormal nervous impulses from the site of injury which prevents spontaneous recovery in traumatic shock (unaccompanied by hæmorrhage), and that if these impulses are controlled, this favourable reaction takes place naturally. The one therapeutic measure (they state) which succeeded in raising and maintaining blood pressure in a traumatized cat when the pressure had fallen to 20 millimetres of mercury was the induction of spinal anaesthesia. They add that there is no doubt that this procedure has a most favourable influence in delaying and even preventing the onset of shock, since, as they point out, spinal anaesthesia blocks all afferent paths, both somatic and sympathetic.

In 1933 Freeman, as already observed, formulated the theory of the hyperactivity of the sympathetic nervous system in shock, with loss of blood volume, following persistent vasoconstriction. Regarding this loss of blood volume, Freeman writes:

In order to account for the loss of blood volume in shock, Starling (*Arch. Med. Belges*, 1918) suggested that the muscle capillaries were dilated and the fluid elements of the blood escaped from these dilated vessels. The effects which have been here obtained may have been due to vasodilatation in the muscles, rather than to vasoconstriction in other areas.

McDowall (1941) writes:

There is no hard and fast line between the unconsciousness of fainting and that of shock . . . It is generally agreed that the fall in blood pressure [in fainting] is due to a dilatation of vessels somewhere, but evidence as to which vessels are dilated is somewhat circumstantial . . . The best direct evidence on this point is . . . that of John Hunter, who . . . when bleeding a patient, observed that the venous blood turned bright red just before the patient fainted. Since the skin vessels were presumably constricted, we must conclude that there was a dilatation of the vessels of the muscles.

DISCUSSION.

From the foregoing survey of the physiology of the circulation and of the recorded clinical and experimental phenomena of shock, it appears that when the body receives any serious injury, an excessive number of afferent stimuli from the injured area reaches the sympathetic nervous system via the brain and spinal cord. The sympathetic nervous system normally reacts to this over-stimulation by constriction of the cutaneous and splanchnic blood vessels, and by dilatation of the blood vessels of the skeletal muscles, the net result of which (after, it may be, a preliminary rise) is, as a rule, a fall in blood pressure. When the stimuli are sufficiently severe, this fall in blood pressure occurs immediately and symptoms of collapse appear at once (so-called "primary"

shock); but when the stimuli are less severe, their effect is cumulative, the fall in blood pressure is more gradual, and collapse appears only after a certain interval of time (so-called "secondary" shock).

Owing to capillary dilatation and diminished blood pressure, capillary stasis ensues. This in time leads to asphyxiation of the capillary endothelium from want of oxygen, with resultant exudation of plasma and loss of blood volume. A vicious cycle is thus established, which, if not broken within two or three hours, inevitably ends in death. While this vicious cycle is in operation, the introduction of any additional stimuli of the sympathetic nervous system (such as pain, fear, cold, anxiety), as well as the reduction of blood volume by hæmorrhage, sweating or vomiting, will still further increase the state of collapse.

Definition of Shock.

Shock may therefore be defined as the collapse of the circulation from over-stimulation of the sympathetic nervous system, which, according to McDowall (1933), if severe, may lead to death from oxygen want.

Treatment.

Since all the symptoms of shock are directly referable to over-stimulation of the sympathetic nervous system and to consequent asphyxiation of the cells of the body through want of oxygen, and since Freeman (1933) has shown that when the sympathetic nervous system is paralysed by ergotoxine, intravenous injection of adrenaline does not cause a fall in blood pressure, I have suggested that shock can probably be successfully treated in its earlier stages (before irreparable damage has been done to the capillary endothelium through tissue asphyxiation) by therapeutic doses of ergotoxine ethanesulphonate ($\frac{1}{100}$ to $\frac{1}{50}$ of a grain), together with inhalation of heated oxygen, in addition to the usual measures (Tomb, 1937).

This probability, based on purely theoretical considerations, receives support from the recent successful employment of ergotoxine in therapeutic doses as an antidote to the lethal effects of scorpion toxin, part of which is a strong stimulant of the sympathetic nervous system (Hassan and Mohammed, 1940).

McDowall (1940) also writes of the "possible desirability of reducing sympathetic activity (in shock) by pharmacological agents", by which it is assumed that he refers to ergotoxine.

General Anæsthesia.

For the induction of general anæsthesia in shock, the inhalation of a mixture of nitrous oxide gas, ether and oxygen is to be preferred to that of ether or chloroform alone, since the oxygen tends to diminish or prevent any increase in the prevailing tissue asphyxiation. O. H. Robertson writes as follows:

[In shock] gas and oxygen [anæsthesia] seems to be . . . the best. Under [this] anæsthesia the patient's general condition may be even better by the end of the operation than it was at the beginning. Operations under ether or chloroform . . . may bring about a return of collapse . . . By using gas and oxygen it is possible to operate with safety in cases whose condition is of such severity that operation under ether or chloroform would be highly dangerous. (National Health Insurance Medical Research Committee, Special Report Series, Number 25.)

Cuthbert Wallace states that: "gas and oxygen was found to be the least noxious [anæsthetic] and with its wider adoption post-operative shock greatly diminished" (National Health Insurance Medical Research Committee, Special Report Series Number 26).

In an article on the relationship of nitrous oxide anæsthesia to anoxia, McCarthy (1941) writes as follows:

A blood-pressure falling below 100 systolic [in nitrous-oxide anæsthesia] with a corresponding decrease in pulse pressure, should always be regarded as a sign of anoxia. A similar picture may be produced by surgical shock, but it is easy to differentiate the one [condition] from the other by . . . increasing the oxygen [supply]. If anoxia is present

[without shock] there will be an immediate return of blood pressure to its normal level . . . In congestive heart failure and in shock there is a stagnant anoxia that [will] be increased by . . . reduction in the oxygen intake . . . In hæmorrhage and anæmia, where there is a reduction . . . in the oxygen-carrying capacity of the blood, more oxygen must be given.

Concussion.

Concussion is described by Romanis and Mitchiner (1937) as follows:

Concussion is a clinical condition which is . . . very similar to that of acute shock, the symptoms in this case being produced by violence acting directly upon the brain, instead of being due to impulses transmitted thereto by afferent nerves . . . The symptoms vary according to the severity of the violence and to whether only the higher centres are affected or the lower medullary centres are involved as well.

According to Miller (1927), of the Department of Physiology and Experimental Medicine, McGill University, who made an exhaustive study of experimental concussion in animals, the symptoms of concussion are mainly referable to the cortex, to the medulla, and to a certain degree to the labyrinth (vertigo). The cortical symptom is the instantaneous generalized disturbance of consciousness, while the medullary symptoms depend on the severity of the blow, and are evidenced either by stimulation or by inhibition of the medullary centres, causing changes in blood pressure, pulse rate and respiration. Miller found that any agency which stimulates or inhibits the medullary centres produces effects similar to those produced by blows on the head. In mild cases of concussion scarcely any stimulation or inhibition of the medullary centres is to be observed. Mechanical effects not severe enough to paralyse the respiratory centre will stimulate respiratory movements. In such cases there is a primary fall of blood pressure (due to vagal stimulation) followed quickly by a rise of blood pressure due to stimulation of the vasomotor centre. The same results are always obtained whether the stimuli affecting the medulla are mechanical, electrical or nutritional. All such agencies act as stimuli of the medullary centres when of moderate degree, but inhibit or paralyse them when severe.

The first centre to be paralysed is the respiratory centre. The vasomotor centre is extraordinarily resistant to violence. From his experiments Miller concluded that concussion is an immediate transient disturbance of consciousness (with or without cell death) caused by direct mechanical violence to the cells of the brain, and that the medullary effects (when present) are those of stimulation or paralysis of the respiratory, vagus and vasomotor centres, according to the severity of the violence.

Gray and Parsons (1912) also found that concussions to the mastoid by hammer acted as stimuli to the vasomotor centre, and that such concussions had a deleterious effect on the central nervous system in proportion to their violence.

Such being the case, in concussion as generally met with, two sets of phenomena are observed: the phenomena of disturbance of consciousness and the phenomena of over-stimulation of the medullary centres. When the stimulation of the medulla is very great, respiratory paralysis occurs immediately and death results at once; but when the stimulus, though severe, is of lesser degree, the vasomotor centre is over-stimulated, with resulting initiation of the syndrome of shock.

Shock in concussion is therefore due to direct mechanical over-stimulation of the sympathetic nervous system (vasomotor centre), all other forms of collapse from trauma unaccompanied by hæmorrhage being due to over-stimulation of the sympathetic nervous system through afferent nerves.

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TUBERCULOUS LESIONS FOUND AT 1,500 AUSTRALIAN AUTOPSIES.

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At the post-mortem examinations made by me at the Royal Adelaide Hospital and at the Mental Hospital, Parkside, a special search is always made for any possible tuberculous lesions, active or healed. Entries of the results are made on cards; a white card indicates that no such lesion was detected, a blue card that tuberculous lesions were present, and a salmon-coloured card that lesions of a doubtful nature were found. The tabulation of these cases has been proceeding for fifteen years or more and some of the previous findings have been published. The present paper comprises the results obtained from the last 1,500 cards. To make certain that a reasonable search for tuberculous lesions has been made, I have used only cards dealing with my own cases. The series, therefore, is perfectly uniform, inasmuch as only one observer is concerned in its compilation. When a card is placed under the heading "Free from Macroscopic Evidence of Tuberculosis", this does not, of course, mean that there were certainly no tuberculous lesions present in the subject. It does, however, mean that if such a person had at one time been infected, such infection was so quickly overcome as to leave behind no obvious naked-eye evidence of its presence, and one can probably infer also that it caused no disturbance of the person's health. It should also be remembered that, though reasonable care was taken, probably healed and even active tuberculous lesions must have been missed in a certain number of cases.

In 1,014 of the 1,500 cases no naked-eye evidence of tuberculosis was discovered. This gives a percentage of 67.4. The doubtful lesions met with in 80 cases amount to 5.4%. If half of these are credited to the subjects free from tuberculosis, one finds that about 70% of the adult community in South Australia coming to autopsy are free from obvious tuberculosis, active or healed. Tuberculous lesions, healed or active, were present in 406 cases—a percentage of 27.2—and if half of the doubtful lesions are added, the percentage will be 30. Of the tuberculous lesions, almost exactly half appear to be completely healed and calcified. If one can consider these figures as an index of the state of affairs in the adult population of Adelaide, then one can say that about 30% of the population have or have had tuberculous lesions, but in only 15% will they be still active at the time of death. This statement perhaps somewhat exaggerates the incidence of tuberculosis amongst the living, because a certain number of the patients who die at the Royal Adelaide Hospital will have entered hospital suffering from tuberculosis, so that the results are somewhat loaded and are not quite a random sample of the population. Nevertheless the figures are probably approximately correct.

BIRTH PLACES OF THE SUBJECTS.

The country of birth of 1,130 of the 1,500 subjects has been entered on the cards. In the case of those not born in Australia, the duration of residence in South Australia is recorded in the post-mortem book, but has not been transferred to the cards. The information is thus available if wanted. The figures given in Table I show that there is a slightly greater tendency for a person born in the British Isles to show manifest tuberculous lesions than one born in Australia.

CARCINOMA AND MITRAL STENOSIS IN TUBERCULOUS AND NON-TUBERCULOUS PERSONS.

Carcinoma.

Of 1,014 non-tuberculous persons, 138 (13.6%) had carcinoma. Of 406 tuberculous persons, 54 (13.3%) had carcinoma.

TABLE I.

Birthplace.	822 Subjects with No Evidence of Tuberculosis.		308 Subjects with Evidence of Tuberculosis.	
	Number.	Percentage.	Number.	Percentage.
Australia	642	78.0	223	72.4
British Isles ..	134 ¹	16.3	68	22.1
Elsewhere	46 ²	—	17	—

¹ England 97, Scotland 21, Ireland 14, Jersey 1, Wales 1.

² New Zealand 3, Germany 12, Sweden 8, Norway 4, Italy 3, Greece 4; one each in Finland, Russia, Bohemia, Holland, Cyprus, Malta, Madeira, Mauritius, India, China, Japan; one born at sea.

Mitral Stenosis.

Of 1,014 non-tuberculous persons, 26 had mitral stenosis. Of 406 tuberculous persons, two had mitral stenosis.

Comment.

From these figures it is seen that carcinoma is just as prevalent in the non-tuberculous as in the tuberculous subject. Mitral stenosis, on the other hand, is rare in tuberculous persons; this supports the view often expressed that for some reason a person with mitral stenosis—a condition usually acquired in childhood or adolescence—is protected to a certain extent from contracting pulmonary tuberculosis.

TUBERCULOUS ULCERS OF THE INTESTINE AND TUBERCULOUS LARYNGITIS.

In 24 out of the 58 cases of extensive pulmonary tuberculosis, and in three out of 18 cases of moderate pulmonary tuberculosis, the swallowed tubercle bacilli had given rise to ulcers in the intestine. This makes a total of 27 out of 76 examples of tuberculosis of the lungs.

There were nine instances of tuberculous laryngitis in the 58 cases of extensive pulmonary tuberculosis and none in the 18 moderately severe cases.

TUBERCULOUS MENINGITIS.

There were 17 examples of tuberculous meningitis amongst the 202 persons with active tuberculous lesions. Of these, two were amongst the 58 cases of extensive pulmonary tuberculosis, three amongst the 18 cases of moderately severe pulmonary tuberculosis and 12 amongst the 33 cases of tuberculosis not essentially pulmonary. The ages of the subjects (in years) were as follows: 15, 17 (2 subjects), 19, 21, 22 (3 subjects), 23, 24, 27 (3 subjects), 28 (2 subjects), 41, 42, 57.

AMYLOID DISEASE.

There were five examples of amyloid disease.

THE MEANS OF ENTRANCE AND OF SPREAD OF TUBERCLE BACILLI IN THE BODY.

In a consideration of the distribution of the lesions in tuberculosis, the means of their conveyance is not always realized. When tubercle bacilli enter the blood stream through ulceration into a vessel, or when they escape into the air passages from a focus in the lung, the distribution of the bacilli can be readily realized. What perhaps is not sufficiently borne in mind is that the tubercle bacillus, being non-motile, can go only where it is carried, and the only usual means of conveyance seems to be either being carried along in a flush of fluid or being taken up by phagocyte cells and carried by them. Except for the accidental introduction of tubercle bacilli into wounds, the usual means of entrance into the tissue spaces must also be by means of phagocytes, probably the macrophages in particular. The phagocytes are always scavenging in the tonsillar and pharyngeal regions and throughout the respiratory tree. In the alveoli of the lung the macrophages pick up carbon pigment, silica particles, tubercle bacilli and other particulate matter that escapes being caught in the mucus lining the upper air passages. The cell with its burden may be expelled by the bronchi, or

the cell may make its way back into the framework of the lung. The same course of events may occur in the retro-pharyngeal tissues. If the burden is a tubercle bacillus, the cell may eventually be overcome by the organism, and will then be engulfed by reticulo-endothelial cells and so start a tuberculous focus. The distance it travels in the tissue spaces and the lymphatics before it comes to rest will vary. In some instances it is probable that the macrophage may even enter the blood stream by the thoracic duct before it becomes "sick". In such a case it may reach any part of the body before the cell comes to rest; thus primary tuberculous lesions may occur in the brain, in the kidney or almost anywhere, the lungs included. In adults the distance to be travelled before the blood stream is reached will obviously be longer than in children.

Once a tuberculous focus has been established, it becomes, of course, a means of seeding tubercle bacilli elsewhere. The tubercle bacilli from a focus must again be carried elsewhere, and here again it is the phagocyte, probably the macrophage in particular, which picks up the organism and transports it. If a reacting barrier of dense fibrous tissue is quickly laid down around a tuberculous focus, its very density will prevent phagocytes from reaching the tubercle bacilli, or if they do, from escaping from the focus. The older the patient, probably the greater the tendency to the formation of dense fibrous tissue. The distribution of tubercle bacilli must be considered in the light of these considerations. Amongst cases of tuberculosis not chiefly pulmonary, examples occur which suggest that tubercle bacilli have been arrested primarily in such organs as the suprarenal gland or the kidney, though usually these locations are part of the distribution from a focus elsewhere.

RESULTS.

Total Post-Mortem Examinations.

Subjects free from macroscopic evidence of tuberculosis	1,014 (67.4%)
Tuberculous lesions present	406 (27.2%)
Lesions of doubtful nature present	80 (5.4%)
Total	1,500

Lesions Presumably Healed.

Calcified areas in bronchial, tracheal or mediastinal glands	107
Calcified mesenteric glands	26
Calcified areas in bronchial gland, kidney and spleen	1
Gritty particles, scars <i>et cetera</i> in one or both lungs	45
Gritty particles <i>et cetera</i> in lungs and calcified areas in bronchial or tracheal glands	17
Gritty particles <i>et cetera</i> in lungs and calcified mesenteric glands	2
Fibrosed cords (possibly silicotic) in lungs with calcified mesenteric gland	1
Healed lesion in lumbar vertebra, scars of old double psoas abscesses (M.73)	1
Healed lesion in dorsal vertebra (F.42)	1
Healed lesions in dorso-lumbar vertebrae, calcified areas in tracheal glands and below right apex (F.61)	1
Right kidney removed 20 years earlier for tuberculosis, calcified glands in superior mediastinum and hilum of liver (F.53)	1
Old tuberculous hip with scars, pleura thickened at apices	1
Total	204

¹M: male; F: female; the figures following in the same parentheses are the subject's age in years.

Total Subjects with Tuberculous Lesions.	
Lesions presumably healed	204
Lesions still active	202
Total	406

Active Tuberculous Lesions Present.

Active lesions in thoracic or abdominal glands ..	31
Healing (?) lesions in lungs	35
Extensive pulmonary tuberculosis with cavitation ..	58
Tuberculous pleurisy with effusion	1
Moderate pulmonary tuberculosis	18
Slight pulmonary tuberculosis	25
Tuberculosis—not chiefly pulmonary	33
Site of lesion not stated	1
Total	202

Active Lesions in Thoracic or Abdominal Glands.

Caseous or still active foci in bronchial or tracheal glands	28
Caseated or caseo-calcified mesenteric glands ..	3
Total	31

Possibly Healing Lesions in Lungs.

Small caseous or caseo-calcified foci in lungs ..	25
Small caseous or caseo-calcified foci in lungs with caseation or calcification in thoracic glands ..	8
Small caseous or caseo-calcified foci in lungs with calcified mesenteric gland	1
Thickened patches in pleura at apices with giant cells	1
Total	35

Extensive Pulmonary Tuberculosis with Cavitation.

Extensive pulmonary tuberculosis with cavitation ..	19
Extensive pulmonary tuberculosis with cavitation and amyloid disease	1
Extensive pulmonary tuberculosis with cavitation and ulcers of intestine	9
Extensive pulmonary tuberculosis with cavitation, ulcers of intestine and amyloid disease .. .	1
Extensive pulmonary tuberculosis with cavitation, ulcers of intestine and tuberculosis of larynx ..	6
Extensive pulmonary tuberculosis with cavitation plus tuberculous meningitis	2
Extensive pulmonary tuberculosis with caseation but no cavities (one with tuberculous pleurisy)	3
Extensive pulmonary tuberculosis with cavitation plus caseous or calcified bronchial or tracheal glands	3
Extensive pulmonary tuberculosis with cavitation, caseous glands, plus ulcers in intestine. . . .	2
Extensive pulmonary tuberculosis with cavitation, caseous glands, ulcers in intestine, plus caseo-calcified mesenteric gland	1
Contracted left lung, tuberculous pleurisy and caseous foci in bronchial gland	1
Extensive pulmonary tuberculosis, ulcers of intestine, tuberculous laryngitis, caseating mesenteric glands and amyloid disease ..	1
Extensive pulmonary tuberculosis with cavitation plus tuberculous epididymitis	1
Extensive pulmonary tuberculosis with cavitation and tuberculous kidneys	2
Extensive pulmonary tuberculosis with cavitation, ulcers of intestine, tuberculous laryngitis and calcified mesenteric glands	1
Extensive pulmonary tuberculosis with cavitation, tuberculous peritonitis, caseating abdominal glands, plus tuberculosis of body of testis ..	1
Pulmonary tuberculosis with apical fibrosis and caseation, ulcers of intestine, plus tuberculosis of left kidney, ureter and bladder	1

Chronic fibroid tuberculosis, ulcers of intestine, and tuberculous glands of neck	1
Pulmonary fibrosis with caseation, ulcers of intestine, tuberculous laryngitis, and caseating mesenteric glands	1
Extensive fibrosing pulmonary tuberculosis with small cavities, and tuberculous cervical, tracheal and bronchial glands	1
Total	58

Tuberculous Pleurisy with Effusion.

Tuberculous pleurisy with effusion (three and a half pints) in half-caste aboriginal	1
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Moderate Pulmonary Tuberculosis with or without other Lesions.

Moderate Pulmonary Tuberculosis.

Peribronchial caseation on right side (M.49).	
Silicosis with extensive miliary tuberculosis added (M.65).	
Small cavity near right apex with extensive consolidation and caseation below and groups of miliary tubercles (M.48).	
At both apices grey fibrosed patches, becoming excavated on right with radiating miliary tubercles (M.60).	
Large caseous patch with giant cells in left upper lobe (F.90).	
Caseated and fibrosed nodules at right apex and in middle lobe. Lower lobe of left lung consolidated with miliary tubercles (M.65).	
Total: 6.	

Moderate Pulmonary Tuberculosis with Tuberculous Meningitis.

Small caseous focus with miliary spread; tuberculous meningitis (F.28).	
Small caseous focus and small cavity near left apex, miliary tuberculosis of lungs, ulcers of intestines, recent tuberculous peritonitis, tuberculous meningitis (F.19).	
Caseous foci near hilum of left lung with tubercles between; tuberculous ulcers of intestine; tuberculous meningitis (M.22).	
Caseous foci in tracheal and bronchial glands, minute-old focus at right apex, tuberculous meningitis.	
Total: 4.	

Moderate Pulmonary Tuberculosis with Lesions in the Glands.

Scattered caseous foci with early cavities at apices, probably tuberculous bronchopneumonia at bases; calcified speck in bronchial gland (M.77).	
Scars at both apices, gritty particle in one; in middle of upper lobe of left lung, small area of caseation and cavitation, in the lower lobe a hard infiltrated area; left tracheo-bronchial glands caseous; carcinoma of stomach (M.76).	
Scarring below right apex with tubercles; agglomerated tubercles in both lower lobes; caseous foci in bronchial and tracheal glands (M.49).	
Small caseous focus in middle of upper lobe of right lung; adhesive caseous pericarditis; large caseous tracheal glands on right (M.23).	
Scattered caseous foci in lungs, some massed tubercles; cavity with hæmorrhage two inches below left apex; caseous foci in tracheal and bronchial glands (M.27).	
Extension to hilum of left lung posteriorly from caseating left bronchial and tracheal glands; miliary blood seeding of lungs, some tubercles in kidneys (M.40).	
Caseous patch in lower border of upper lobe of left lung, another one and a half inches below apex of lower lobe of right lung; caseous foci in tracheal glands (F.27).	

Tuberculous nodules in spleen and liver, massed miliary tubercles in lungs, miliary tubercles in spleen, kidneys and liver; ulceration of intestines (M.13).

Total: 8.

Slight Pulmonary Tuberculosis.

Slight pulmonary tuberculosis 21

Slight pulmonary tuberculosis with calcification in tracheal or bronchial glands 4

Total 25

Typical Cases.

Small cavities with fibrosis at right apex, (?) quiescent (M.59).

White patch, microscopically tuberculous, in upper lobe of right lung towards the hilum; death from lobar pneumonia (M.42).

Small firm grey area, with calcified centre in middle of lower lobe of right lung; death from rupture of syphilitic aorta into pericardium (M.30).

One inch below the left apex an infiltrated area, probably tuberculous, the size of a pea; one inch and a half below the right apex, a small caseous patch and cavity, the size of a pea, with fibrosis around; death from extensive burns, acute mania (F.59).

Caseous focus, size of a marble, with two or three smaller ones above it in lower part of upper lobe of right lung; death from empyema (four pints of foul pus), pericarditis and pneumonia (M.55).

Total: 25.

Tuberculosis not Chiefly Pulmonary.

Kidneys, each epididymis, caseated tracheal gland, caseous foci near left apex, gritty particle near right (M.19).

Kidneys, right epididymis, caseated tracheal gland, miliary tuberculosis of lungs (M.66).

Right kidney, each epididymis, vesiculæ, groups of tubercles in fibrous strands in middle of right upper lobe, tuberculous meningitis (M.42).

Each epididymis, prostate and vesiculæ, caseating focus near right apex, miliary tuberculosis of lungs, tuberculous meningitis (M.28).

Left kidney, bladder and prostate, tuberculous peritonitis, group of cavities below left apex (M.34).

Right epididymis and vesiculæ, mesenteric, bronchial and mediastinal glands, pea-sized caseous focus in right lung, ulcers in intestine, miliary tuberculosis, tuberculous meningitis (M.17).

Vesiculæ, miliary tubercles and streaks in kidneys, caseous foci in bronchial glands, intense miliary tuberculosis of lungs, tuberculous meningitis (M.24).

Miliary tuberculosis of peritoneum, more plaque-like in pelvis, no primary focus found (M.77).

Caecum, three superficial tuberculous ulcers; death from cerebral softening (F.27).

Caecum with several tuberculous ulcers, caseous mesenteric and left bronchial glands; death from bedsores and wasting; mental patient (F.53).

Caseating mesenteric glands, tuberculous gland in front of root of left lung, old scarred tuberculosis with calcified specks below both apices and lower down several small more active foci, tuberculous meningitis (M.57).

Adhesive caseating tuberculous peritonitis, caseating tracheal glands, caseating focus in middle lobe of right lung (M.19).

Tuberculous meningitis, primary focus not found (M.23).

Right bronchial and tracheal glands (extensive caseation), miliary tubercles in both pleurae, a few in kidneys and spleen, tuberculous meningitis (F.21).

Caseated broncho-tracheal glands, miliary tuberculosis of lungs, spleen, kidneys, tuberculous meningitis (M.17).

Caseation in lower cervical and tracheal glands, lymphatic extension to hilum of left lung, two tuberculomata and large tuberculous abscess in liver, tubercles and tuberculous plaques on peritoneum (F.55).

Caseous glands in neck from bifurcation of carotid to adherent apex of right lung, which is fibrosed (Negro, M.64).

Caseated glands in anterior triangle of neck and root of right lung; death from (?) tetanus; glands also permeated with carcinoma cells, but no primary focus detected (F.63).

Right bronchial glands (caseated foci), two small tuberculomata in cerebellum, miliary tuberculosis of lungs, kidneys, massed tubercles in thyroid, tuberculous meningitis (F.27).

Caseated glands in neck, caseated mediastinal and bronchial glands, intense miliary tuberculosis of lungs, less severe in liver, spleen and kidneys (F.3).

Both suprarenals, right kidney (F.59 and M.48).

Both suprarenals, left kidney, right epididymis, prostate, old calcified focus in upper lobe of right lung, miliary tubercles in liver (M.54).

Both suprarenals, both Fallopian tubes, calcified speck near left apex (F.58).

Both suprarenals, lower dorsal vertebrae with double ilio-psoas abscesses, cold abscess (one pint) in right subpectoral region with caseous focus in sternum (M.57).

Both Fallopian tubes, caseous endometritis, several small old foci in lungs with recent miliary seeding, extensive ulceration of intestines, tuberculous laryngitis (F.42).

Right Fallopian tube, secondary tuberculous peritonitis, small cavities and caseating foci at left apex, early tuberculous ulcers of intestine, miliary tuberculosis, tuberculous meningitis (F.27).

Both Fallopian tubes (removed six months earlier), puckering at apices of lungs, calcified nodules at right apex, tuberculous meningitis (F.27).

Tuberculous right *otitis media*, left tuberculous pleurisy, small caseous foci near bases of both lungs and in tracheal gland, miliary tuberculosis of spleen, liver, kidneys, lungs, tuberculous meningitis (M.15).

Tuberculous hip with sinuses (25 years), scattered caseous foci in lungs and spreading tubercles, ulcers of caecum, amyloid kidneys (M.36).

Tuberculous hip, caseous specks in right bronchial and mediastinal glands, Fallopian tubes (?), amyloid disease (F.22).

Right ulna extending to elbow joint, calcified mesenteric glands, miliary tuberculosis of lungs, carcinoma of oesophagus (M.57).

Caries of deep surface of sternum, massive caseation extending into right lung, caseous foci in right lung and smaller ones in left, older focus at left apex, tuberculous pericarditis, ulcers of intestines (M.30).

Total: 33.

Lesions of Doubtful Nature.

Thickened pleura at apex or apices, or thickened cartilaginous cords: 13. (Probably tuberculous 1, possibly tuberculous 3, probably not 8, no opinion 1.)

Scar tissue or thickened areas at or near the apex or indefinite thickening, no caseation or gritty particles: 27. (Probably healed tuberculosis 4, possible or doubtful tuberculosis 12, probably not 9, no opinion 2.)

Small gritty particle or fibrotic nodule *et cetera*, elsewhere than near apices: 12. (Probably healed 1, possible 8, probably not 3.)

- Several scattered caseo-calcified areas (M.75): 1. (Possible 1.)
 Calcified specks on pleura: 2. (Possible 1, very doubtful 1.)
 Extensive dense silicosis, one with cavity: 5. (No evidence of tuberculosis 5; guinea-pigs inoculated from 2, including one with cavity.)
 Small silicotic nodules: 2. (No giant cells microscopically 2.)
 Subpleural silicotic nodules and some diffuse fibrosis: 2. (One possible, one probably not.)
 Silicotic thickening of septa: 1. (Probably only silicosis.)
 Some diffuse fibrosis: 1. (Probably not 1.)
 Tracheal, mediastinal or bronchial glands, fibrosed or necrosed areas microscopically: 10. (Probable 3, possible 4, probably only silicotic 3.)
 Putty-like material in ileo-colic gland: 1. (Probable 1.)
 Kidney, necrotic focus microscopically suggestive: 1. (Probable 1.)
 Upper dorsal vertebra, (?) old collapse: 1. (Probable 1.)
 Site and degree of lesion not stated: 1.
 Total: 80.

Summary of Opinions on Doubtful Lesions.

Probable tuberculosis	12
Possible or doubtful tuberculosis	30
Probably not	34
No opinion	3
Site and degree of lesion not stated	1

Reports of Cases.

RUPTURED AORTIC ANEURYSM IN A YOUTH AGED SIXTEEN YEARS.

By HAMILTON PATTERSON, M.B. (Edinburgh),
 Ipswich, Queensland.

At a post-mortem examination I performed recently the findings were sufficiently unusual for me to think them worthy of being placed on record.

Clinical Record.

V.B., aged sixteen years, a youth employed at the Salvation Army Farm at Riverview, Queensland, was found dead at stool in an earth closet on November 27, 1941. So far as was known, the boy had never been ill, but, being considered weakly, he had always been given light work.

Post-Mortem Findings.

The subject was a tall, thin youth. The chest was distended as though he had been an asthmatic. When the ribs were sawn through there was a sudden gush of yellow fluid of the consistency of water from the pericardial sac. There was about one pint of this fluid, and the pericardial sac contained in addition a large quantity of blood clot. On the anterior aspect of the first part of the aorta there was a bruised-looking area about the size of a five-shilling piece. Closer inspection showed this area to be almost as thin as paper, and portion of it had ruptured, exhibiting a hole the size of a pea. The heart was otherwise normal. No calcareous plaques in the aorta were visible to the naked eye. The abdomen contained a typical "nutmeg" liver, the right lobe extending right down to the right groin.

Comment.

A case is reported of the sudden death of a youth, aged sixteen years. The post-mortem examination revealed that death was due to the rupture of a dissecting aneurysm on the anterior aspect of the first part of the aorta. The primary cause must almost certainly have been congenital syphilis. The rupture was apparently caused by the effort of straining at stool.

Reviews.

WAR SURGERY.

FURTHER consideration of war injuries of the ear—very largely the effects of blast upon the tympanum—is given in the first pages of Part V of "Surgery of Modern Warfare".¹ It is pointed out that bleeding from this cause, if associated with concussion, may lead to an erroneous diagnosis of fracture of the base of the skull.

In the following chapter—upon wounds of the air passages and air sinuses—a field is explored which concerns both the specialist and the general surgeon. The latter, however, has to deal unaided with wounds of the neck. This is a region full of difficulties and dangers. So real are these difficulties that the editor, for reasons which he details, found it incumbent upon himself to contribute this chapter. He contrives to make it both interesting and helpful, with advice as to the best methods of dealing with the almost inevitable hæmorrhage. The dangers of delay, reactionary or secondary hæmorrhage, are stressed. Intravenous anaesthesia, free exposure with division of the sterno-mastoid, and an orderly plan of campaign all contribute towards command of the situation.

Section X deals with the subject of wounds of the central nervous system and its coverings. The first chapter—upon injuries of the brain and skull—is by Norman Dott, whose description of the methods employed for the diagnosis, surgical treatment and general management of these cases is admirable. It is a description of the handling of a special type of injury by a surgical specialist, with all his accustomed aids and facilities, based upon the thesis that patients so affected travel well and should be evacuated to a centre where adequate staff and equipment are available. Nevertheless the general surgeon who perforce is called upon to deal with such patients will find a great deal of help and guidance in these pages, particularly those dealing with assessment, diagnosis and decision. A surprising omission is any reference to the indications for removal of a projectile lodged within the brain substance. The important principle of "borrowing" sound scalp to cover defects in bone and brain might well be illustrated by diagram.

The chapters which follow deal with injuries of the spine and cord and convey an excellent picture of the march of neurological phenomena leading to the development of the automatic bladder in total lesions. The signs indicative of incomplete lesion are well described.

Ogier Ward contributes a chapter upon the management of the bladder in these cases. This chapter is a most valuable one, being an authoritative and well-reasoned statement of this outstanding problem. The pros and cons of suprapubic cystostomy are discussed in relation to the development of the automatic bladder, "once the pride and joy of the urologist". The method of automatic tidal drainage of the bladder introduced by Munro, of Boston, is well described and illustrated.

Section XI is given up to a description of surgical diseases of subtropical countries, amebiasis with liver abscess, bilharziasis *et cetera*.

Section XII is concerned entirely with organization and administration, naval, military and civil "E.M.S." Based as it is upon recent experiences in these several fields, this section has a particular appeal at the present time and well repays close study.

The final section consists of an appendix in which is found a considerable number of short articles dealing, *inter alia*, with such subjects as shock, blast, burns, chemotherapy, wound excision, gas gangrene, and some further notes on blood and plasma transfusion. All are really well done, and that upon gas gangrene will differentiate, for those who are unfamiliar with the clinical forms, the grave from the less dangerous manifestations of gas infection. Renewed attention is given here to the controversial question of the value of X-ray treatment of this condition, a question which is urgently in need of final decision, and upon which the editor prefers to withhold judgement. In this he gives further evidence of the wisdom he has displayed throughout in the compilation of this monumental work, now completed, the "Surgery of Modern Warfare".

¹ "Surgery of Modern Warfare", edited by H. Bailey, F.R.C.S.; Part V; 1941. Edinburgh: E. and S. Livingstone. Super royal 8vo, pp. 235, with illustrations and diagrams. Price: 17s. 6d. net.

The Medical Journal of Australia

SATURDAY, FEBRUARY 28, 1942.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: Initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

PHYSICAL FITNESS AND EFFICIENCY.

IN January of last year under the heading "Physical Fitness and Its Determination" reference was made in these columns to the examination and acceptance of recruits for enlistment in the armed forces. Mention was also made of an important communication by H. H. Kessler, of Newark, New Jersey, regarding the determination of physical fitness from both the military and the industrial points of view. Kessler regarded physical fitness as a socio-economic concept involving the social evaluation of a series of anthropological, physiological and psychological traits. He held that false concepts of capacity to work had created vague standards of physical fitness and that these had condemned the physically defective who were handicapped by minor disabilities, but who possessed great potentialities for functional performance. It is probably true that few terms are so vaguely used as the term physical fitness; it is used as though fitness for one occupation or pastime denoted fitness for all others. The incorrectness of such an idea is obvious, whether the term is applied to military or to civil matters. At the present time more is being heard of the need for production in industry than ever before, and if industry is to be productive, those engaged in it must be physically fit for the tasks they have to undertake. That physical fitness has a great bearing on the problem of unemployment has been recognized by workers in South Africa, and we have received recently from the South African Institute for Medical Research a monograph entitled "Training and Efficiency" which should be in the hands of all interested in preventive medicine, in war-time production in industry and in the welfare of workers. The authors of this monograph are Ernst Jokl, E. H. Cluver, C. Goedvolk and T. W. De Jongh, and they describe their investigation as an experiment in physical and economic rehabilitation.

Unemployment is a serious problem in South Africa and apparently many of the unemployed are unemployable. One of the causes for this state of affairs is the low state of physical fitness of a large group of Europeans. (During 1935-1936 there were 118,939 unemployed persons among the Europeans who number a little less than two million.)

During 1933 a special battalion was established "for the purpose of combating the deteriorating influence of unemployment and of providing discipline and training for unemployed boys and young men". The cost for the first year amounted to approximately £80,000, which was shared equally by the Departments of Defence and Labour. The young men recruited were between the ages of seventeen and twenty-two and they had reached a minimum (apparently very low) educational standard. During the period 1933 to 1939 no less than 13,815 young men were accepted; of these 10,735 completed the training course and 9,409 of them were subsequently placed in employment. The "most important" of the training measures adopted was physical training. The special investigation reported by Jokl and his co-workers had to do with thirty-two recruits from this special battalion. The recruits were free from infectious diseases and other gross physical disabilities. At the time of their attestation to the course most of them were unable to find employment. "They made a dull and undisciplined impression. Their posture was lax and their general bearing bad. Most of them came from poor farm homes, and one could safely assume that their nutrition had been unsatisfactory." At the camp these young men for the first time in their lives were subject to a régime of strict discipline. They lived in barracks or well-kept tents and slept in proper beds; they received a well-balanced diet; they had to follow a carefully planned time-table in which ample time was set apart for recreation, and they received three hours of physical training every day. According to the standards laid down by labour and recruiting officers and by the medical authorities of the army these men were fit when they started the course, but they were either unemployed or were working under unsatisfactory conditions; they were really unemployable because the labour market at the time was flooded with demands for workers. Their plight was the result of their low power of endurance, of physical weakness and of poor educational qualifications which made them unfit for anything but manual labour. The observations made during the teaching and training of these young men were extensive. Anthropometric measurements of all kinds were included; the respiratory rate, vital capacity and breath-holding time were observed, the pulse rate and blood pressure were recorded and the performance increase in athletic tests was noted. The findings are set out in tables covering many pages of the monograph. As might be expected, the results were remarkable—in practically every subject there was an improvement in the general standard of physiological and athletic efficiency. The main significance of the study is claimed to be the production of evidence to show that the low standard of fitness and efficiency, which is found in a section of the South African population, is not due to a basic biological defect, but is largely the expression of environmental shortcomings. The conclusion is that physical training, in combination with an educational system conducted under conditions of discipline, and supplemented by a satisfactory nutritional régime, is capable of producing and maintaining a highly satisfactory standard of health and of labour power for practically every European South African.

This study of Jokl and his co-workers is but one in a series. In a first study, published in 1940, they investi-

gated the different racial groups in South Africa and found similar standards of physical performance in the different groups. The present study is the second. In the third it will be shown that "even from an economically poor or almost valueless 'raw material of human labour' training can build up a high potential of production, and thus of individual and communal wealth". The fourth part will deal with administrative steps, for these authors are trying to find ways and means of leading the educational and economic data revealed by their study into "well constructed channels of a coordinated labour effort". Their work is of great importance in regard to the Empire's war effort, for what is true of South Africa in this regard is probably true of other places; it will be of even more importance in the difficult times that will surely follow the cessation of hostilities. The war has shown us what can be accomplished by organized and coordinated action; it has also shown the effect of well-directed discipline. Readers of this journal know that organization and coordination of action are of little value if health is lacking. One of the ways of attaining health is by some system of training and education such as Jokl and those associated with him have described. Many persons have neither the desire nor the initiative to seek any means for the improvement either of their health or of their capacity for work. Quite a number of persons know nothing of the dignity of work, though it is probably true that this number is not so large as it used to be a decade or two ago. Clearly some incentive must come from outside the individual; an intelligent administration will in the days to come supply this incentive, and medicine, if it is worthy of its tradition and its place in the scheme of things, will stimulate the administration.

Current Comment.

THE TREATMENT OF VARICOSE VEINS.

THE embarrassment caused by the disfigurement of varicose veins is one of the most common reasons behind a request for their treatment; but in war-time, with the aggravation of the varicosities by long marches and with the insistence of the Army authorities on remedial treatment before the recruit may be accepted, many of those reporting for treatment are soldiers who are often unwilling to exhibit the patience or have not the time necessary for a long course of injections. The method of ligation of the proximal end of the greater saphenous vein followed by retrograde injection of a sclerosing fluid gives excellent results in most cases and is to be recommended especially for persons with large varicosities and for those in whose treatment the time factor is important. The proximal end of the greater saphenous vein is identified under local anaesthesia, the small collateral veins which converge towards the *fossa ovalis* are ligated, the leg is then elevated for a few minutes to empty the blood from the veins, and then the greater saphenous vein is ligated. Among the sclerosing fluids commonly used are "Ethamolen" and sodium morrhuate. The volume of fluid to be injected depends on the type of solution used and on the size of the varicosities. Six to eight millilitres of "Ethamolen" or eight to twelve millilitres of sodium morrhuate are necessary in the average case. After the vein is ligated the leg is hung over the side of the table and then the fluid is injected into the vein through a cannula attached to a syringe. It is important, especially when using sodium morrhuate, that the wound be packed with gauze, so that if any of the solution is split inadvertently, the tissues of the wound are protected from damage. When the

cannula is withdrawn from the vein care must be taken to prevent regurgitation of the fluid into the tissues. The vein is then ligated distal to the opening for the cannula and divided between the ligatures to prevent recanalization later. The wound is closed with sutures and pressure is applied over the vein with an elastic bandage. The clot should be palpable within a few seconds of the injection, and usually extends throughout the whole length of the vein. This whole procedure may be carried out in ten minutes and usually results in sclerosis throughout the greater saphenous system of veins. If necessary, the lesser saphenous system may be similarly treated at a second operation. Because of the pain sometimes experienced in the few days following operation and due to the chemical phlebitis, and because it is desirable to keep the patient ambulatory, it is recommended that only one leg be treated at the one sitting. In cases which are severe enough to require this operation the presence of varicose ulcers or eczematous lesions are not contraindications to operation; rather they are definite indications, for when once the veins have thrombosed, complications rapidly heal.

The subject of injection of varicose veins has recently been discussed by I. A. Brunstein,¹ who lays great stress on the necessity for emptying the vein before the injection, whether the injections are given into the veins directly or in a retrograde direction after the ligation of the vein. Brunstein draws attention to the frequency with which distressing sequelae, such as pain, discomfort and disability, are often encountered following injection of varicose veins, and suggests details in treatment which may help to lessen these sequelae. These suggestions may be summarized as follows: (i) avoidance of puncturing an indurated, pigmented or eczematous area by starting the injection in healthy tissue; (ii) fixation of the vein by upward pressure over the overlying skin to prevent transfixion of the vein or its displacement by the needle; (iii) introduction of the needle parallel to the long axis of the varicosity, and the selection from a cluster of varices of the varix with the greatest diameter to avoid transfixion of the vessel; (iv) avoidance of transfixion of small invisible subcutaneous varicosities when a large varix is being approached with the needle; (v) insertion of the needle at about one-third of an inch from the vessel to avoid puncture of the skin over the varix (this is imperative during the injection of varices covered with only a thin layer of atrophic skin); and (vi) avoidance of over-distension of the varix with sclerosing solution. Increased resistance to the introduction of the solution with visible bulging of the injected varix is a warning signal to discontinue the injection.

When the injection is given with the vein full, gross thrombus formation with the appearance of painful, hard, nodular masses and extensive edema in the perivenous tissues often occurs. The resulting pain and discomfort and the red indurations often cause limping and do not encourage the patient to continue treatment. Large thrombosed veins are slowly absorbed and are frequently the seat of recanalization. On the other hand, sclerosis by injection into empty veins will cause blocking of the varices by fusion of the opposing surfaces of the vessel and not by gross thrombosis. Recanalization of such closed vessels is less likely, since they undergo organization and absorption more readily. Also the cosmetic result after injection into collapsed veins is superior to the unsightly, discolored indurations produced with distended veins. The chief objection to the employment of the empty technique lies in the theoretical rather than the actual possibility that the sclerosing solution may escape through the communicating veins into the deep venous circulation and damage it. The technical difficulty of the injection of the fluid into an empty vein is easily overcome by insertion of the needle into the distended vein and elevation of the leg before the fluid is injected. Adequate compression is of primary importance to maintain varicosities in a collapsed and well-supported state after the injections. The cosmetic results are better if the support is not confined to the site of the injection, but extends to the uninjected proximal and distal varices as well. This will

¹ The American Journal of Surgery, November, 1941.

guard against the possibility of unsupported thrombosis caused either by retrograde flow of solution or by a possible migrating phlebotic reaction, and thereby will limit and often prevent possible massive thrombosis. The support to the veins may be provided by an elastic bandage, by a zinc gelatine bandage or by adhesive strapping; but whatever is used should be applied with even pressure and strong tension should be avoided.

Even if it is possible to perform local injections without causing discomfort and without troublesome sequelae, ligation and retrograde injection require only one visit to the surgery instead of many, as with local injections, and give more satisfactory end results. Brunstein gives many useful hints for the local injection of varicose veins; but it is surprising that he has not laid more stress on the method of ligation and retrograde injection.

MALIGNANT DISEASE IN SCARS FROM BURNS.

Most of the reported cases of sarcoma in scars have followed lupus or war injuries; but fortunately such a complication is extremely rare. Carcinomata more often supervene in scars, and of these the majority are the squamous-celled carcinoma or basal-celled carcinoma in the scars resulting from burns. Marjolin was the first to describe the pathological picture of malignant disease occurring in scars from burns, and for many years these lesions were called Marjolin's ulcers whether they were in the simple chronic stage or whether they were malignant. Most students are aware of the kangri-burn cancers as an illustration of the relationship existing between long-continued mild irritation and the development of malignant disease. Keloid formation is also a well-recognized complication of burns; but from the text-books on surgery it is easy to make the mistake of regarding these keloids and malignant lesions associated with burns as complications limited to those of negroid ancestry. As with other types of malignant disease, various theories as to their cause have been propounded; but it is possible, as Roffo and Gandolfo suggest, that the development of cancer in a burn scar is the result of isolation of epithelial cell "nests" subsequent to the scarring. These cell "nests" may then remain dormant until irritated by such processes as trauma and endocrine influences. Such a suggestion does not, of course, explain why this complication is not more frequent. An obvious but unlikely explanation for the inconsistency is that there may have existed a precancerous condition of the affected area prior to the injury.

An apparently authentic case of sarcoma developing in an old burn has been reported by R. M. Fleming and P. R. Rezek.¹ The lesion in their case was treated by wide excision with the diathermy knife; but, despite deep X-ray therapy, fatal metastases ensued. Of interest in this case are the facts that although the burn had occurred forty-nine years previously, the lesion had never been completely healed, and that the scar had been severely traumatized (sunburnt) just prior to the onset of the malignant change. In the same journal H. R. Browne² has reported a case of carcinoma occurring in an old burn scar. In this case also healing had been prolonged, but the initiating trauma was represented by several operative attempts to overcome the contracture. By diathermy excision and grafting this patient appears to have been cured. These cases are of interest in view of the large number of burns that are caused under active service and air raid conditions.

RIBOFLAVIN DEFICIENCY.

RIBOFLAVIN belongs to the B₂ group of vitamins. It is a yellow fluorescent pigment, and it is known to occur naturally in eggs, milk and liver. Its chemical name is 6,7-dimethyl-8-ribityl-isalloxazin and its formula C₁₇H₂₀N₄O₆. It is also known as ovoidin, lactoflavin and hepatoflavin (depending on its source) and sometimes merely as flavin.

It is believed to be essential to cellular respiration. Formerly this vitamin was confused with vitamin B₆, which consists of the rat antidermatitis factor and nicotinic acid or pellagra-preventive factor, and other factors of probably less importance. The known vitamins are increasing in numbers so rapidly that it is very difficult to keep track of them. It is time some authoritative body devised a more sensible system of nomenclature. Numbers and letters convey little meaning. But let us return to our discussion of riboflavin. It has been shown in the United States of America that deficiency of riboflavin is apt to lead to stomatitis at the angles of the mouth, cheilosis as evidenced by a reddened denuded condition of the lips, dermatitis in the region of the naso-labial folds and sometimes round the eyes and ears, and superficial keratitis. The symptoms quickly disappear on the exhibition of riboflavin. Little work has been done on riboflavin deficiency in the country where it is most likely to be widespread—India. Therefore W. R. Aykroyd and O. P. Verma have recently carried out an investigation at the Government Ophthalmic Hospital, Madras.¹ They point out that typical Indian rice diets of the poor are deficient in riboflavin. A liberal intake of milk is beyond the means of the poor people of South India; liver is not a usual item of diet. They state that a further rich source of riboflavin is yeast; but they point out that dried yeast is very expensive.

In the course of the authors' investigation numerous patients with angular stomatitis and superficial keratitis were observed. Thirteen were selected for treatment, the number being limited by the restricted amount of riboflavin that was available. The patients were of both sexes and their ages ranged from eight to sixty years. They suffered from a burning sensation in the eyes, mistiness of vision, photophobia and excessive lachrymation. The tongue was fissured, but did not have "the 'magenta' colour described by the American workers as a feature of 'ariboflavinosis'". Cheilosis was not a prominent symptom. All the male patients complained of itching of the scrotum. Examination showed the scrotum to be rough and scaly.

Treatment consisted in the administration of riboflavin by intramuscular injection. The initial dose was usually 2.0 milligrammes. Repeated daily doses of 1.0 to 2.0 milligrammes were given until 5.0 to 24.0 milligrammes had been given, according to the severity of the disease. The subjective symptoms rapidly subsided. The signs of conjunctivitis and keratitis also disappeared within a few days, and corneal opacities diminished. Aykroyd and Verma suggest that in some cases these opacities would vanish if treatment could be continued longer. Fissures of the tongue disappeared after the administration of 10.0 milligrammes of riboflavin. Stomatitis was slower to subside. The skin of the scrotum did not become smooth except in one case, in which 24.0 milligrammes of riboflavin were given.

A remarkable feature of the investigation was the rapidity of the recurrence of symptoms after the administration of riboflavin was suspended. Several patients returned after periods varying from nine to fifteen days, with the same complaints as before treatment. Aykroyd and Verma suggest that this is due to rapid excretion of the vitamin. They quote Swaminathan to the effect that 80% to 90% of riboflavin given orally in doses of 2.0 to 10.0 milligrammes may be excreted in twenty-four hours. After the suspension of treatment the poor Indian returns to a state of riboflavin starvation.

This investigation has something more than a purely scientific interest for Australians. Minor degrees of vitamin deficiency are frequently recognized here. The value of the therapeutic and prophylactic administration of vitamins or vitamin-containing foods has been abundantly proven. And this applies to the group of B vitamins no less than to the others. Frank beriberi and pellagra are of course rare; but thiamin (vitamin B₁) deficiency and nicotinic acid (part of vitamin B₃) deficiency are not. Medical practitioners should bear vitamin deficiency in mind, especially in dealing with poor people and people with capricious appetites or gastro-intestinal disturbance.

¹ The American Journal of Surgery, November, 1941.

² The Indian Medical Gazette, January, 1942.

Abstracts from Medical Literature.

THERAPEUTICS.

The Massive Dose Therapy of Early Syphilis.

D. C. ELLIOTT *et alii* (*The Journal of the American Medical Association*, October 4, 1942) give a progress report on the results and observations of "Mapharsen" therapy in cases of early syphilis under the massive dose method. A total of 968 cases are reviewed, 13% being in the "sero-negative" primary stage, 28% in "sero-positive" primary, and 59% in secondary stages. A total dosage of 1,200 milligrammes of arsenoxide was administered in five days by varying methods (carried out at different hospitals)—slow intravenous drip, rapid intravenous drip and multiple injection. The number of patients treated by these various methods is not sufficiently large to evaluate the benefit of each method. Detailed examinations were made by dark-ground illumination, by the Kahn test, by blood and urine studies, by spinal fluid studies, and by other tests as indicated. Most of the patients have been under observation only for a period of one year, and this point is emphasized in interpretation of results. There was a fatality rate of 0.3%, in each case due to a toxic encephalitis. Other complications of therapy were nausea (60%), primary first-day fever (48%), secondary fever (41%), pain in the arm (41%), headache (31%), toxicodermas (11%). Only two cases of clinical jaundice were seen; the observed peripheral neuritis was transient and mild. There was a complete absence of dermatitis exfoliativa, blood dyscrasias and nitritoid reactions. The clinical and serological trend indicates that the percentage of therapeutic failures occurring within six months to one year after a single course of massive dose therapy will probably be between 5% and 15% when 1,200 milligrammes of arsenoxide are used. The public health importance of a method which offers the possibility of eliminating the infection in at least 85% of early cases with five successive days of treatment and of presenting an opportunity for the rapid control of this disease warrants the continuation of the present study in well-organized treatment centres.

Motor Neurone Degeneration Treated with Vitamin E.

C. WORSTER-DROUGHT AND J. SHAFAR (*The Lancet*, August 23, 1941) report a series of 25 patients suffering from different forms of motor neurone degeneration (progressive muscular atrophy, amyotrophic lateral sclerosis, and progressive bulbar palsy) treated for periods ranging from five to ten months with vitamin E in daily doses of either 18 milligrammes or 30 milligrammes. They review the experimental evidence that has led to the use of vitamin E in these disorders, and discuss the clinical experience of other workers. In this series vitamin E was administered to the patients in two forms—as wheat germ oil capsules equivalent to 18 milligrammes of tocopherol daily, or in the form of synthetic α -tocopherol acetate (30 milligrammes daily). Of the 25 patients, only two showed definite improvement, a third reported his condition as

improved, and slight improvement in gait was noted in the case of a fourth. Progressive deterioration occurred in all nine cases of bulbar palsy. Improved general health and emotional tone were noted in nine instances. The authors consider Bicknell's statement that "vitamin E appears indeed to be one of the great advances in general medicine of the century" appears premature, and that it has not been justified by results hitherto recorded. They conclude that the value of vitamin E therapy in motor neurone degeneration remains speculative, but that in view of the improvement in two of their cases it is worth a further trial.

Bile Secretion and Bile Salt Therapy.

A. C. IVY (*The Journal of the American Medical Association*, October 4, 1941) has investigated the physiology of bile salt therapy to assist the clinician in his treatment. It was shown early that protein stimulates the formation of the bile and bile salts. Fat and carbohydrate seem to lead to a reduction in output so that a mixed diet does not change the output to any marked degree. There is no direct relationship between bile salt output and the caloric value of the diet. It was demonstrated that the rate of bile salt production balances the rate of "destruction" (about 10% cholic acid). With the introduction of six grammes of bile salt a catharsis is produced, and the bile salt output from the liver is reduced until a relatively constant level is reached. In the presence of severe hepatitis cholic acid disappears from the fluid drained from the bile duct; the administration of bile salts does not then cause a cholelithiasis and the administered cholic acid does not appear in the bile. The metabolism of bile salts with complete obstruction of the common bile duct is not yet fully determined. There is no definite evidence that sodium dehydrocholate facilitates the recovery from jaundice due to obstruction and arsenical hepatitis. The production of choleliths by administration of bile salts flushes the bile ducts but not the gall-bladder. However, frequent evacuation of the gall-bladder, in the presence of normal formation of bile, facilitates and speeds the removal of sediment (sand in experiments) from the viscous. Ox bile salts (conjugated unoxidized cholic acid) contains the bile salts found in human bile. Dehydrocholic acid (oxidized unconjugated cholic acid) is definitely hydrocholeric and is non-toxic.

Circulatory Failure in Diabetic Acidosis.

A. E. SCHACTER *et alii* (*The American Journal of the Medical Sciences*, September, 1941) have examined the nature of the failure of the peripheral circulation and its relation to treatment of diabetic coma. A series of eight cases of severe acidosis provided the material for the study. Estimation of serum protein concentration, hemoglobin and cell volume by hematocrit points to a severe dehydration and hemoconcentration. It has been shown that these changes are accompanied by a reduction in blood volume and also suggested that in this series the reduction was at least 600 cubic centimetres. Cold extremities, rapid, thready, low-volume pulse and low blood pressure were seen in these patients. Measurements of the blood flow through the hand indicated the severity of the

reduction of the peripheral circulation. Blood gas analyses in surgical shock reveal a widening of the arterio-venous oxygen difference with a marked reduction in venous oxygen saturation, the latter apparently due to a reduced circulation. When the reduction in blood flow is so great that even very complete removal of oxygen from the blood arriving fails to deliver an adequate oxygen supply per unit of time, tissue anoxia results. This is the stagnant type of anoxia of surgical shock. Patients in diabetic acidosis were found to differ from those in surgical shock with respect to the level of their venous oxygen saturation in the presence of a markedly reduced blood flow; there was little oxygen unsaturation in venous blood suggesting a failure of the hemoglobin to liberate its oxygen to the tissues and a failure of the tissues to remove the oxygen which does arrive. These findings suggest a histotoxic as well as a stagnant anoxia. The suggested theories for this are: inability to utilize carbohydrate, ketosis or acidosis. Any one or all of these may be responsible. When there is a marked reduction in peripheral circulation with a low blood pressure and unconsciousness, the administration of saline or other solutions of electrolytes without colloid osmotic pressure is insufficient to bring about a permanent increase in blood flow and blood pressure. Plasma, blood or acacia should be given early to these patients to ensure maintenance of blood flow. Saline solution given subsequently for the replacement of electrolytes and water will then probably be effectively absorbed and retained. The prompt restoration of the blood volume and its maintenance are just as important as the administration of insulin in diabetic acidosis.

The Treatment of Malaria.

LEONARD ROGERS (*The Practitioner*, June, 1941) epitomizes the modern treatment of malaria. For the febrile stage quinine is still the best drug. The high cost of the pure alkaloid places it beyond the reach of vast numbers of the indigenous population of malarious countries. The Government of India issues a cheap mixture of cinchona alkaloids under the name of cinchona febrifuge. Lately it has also issued the more satisfactory quinetum containing equal parts of the three chief alkaloids of the bark of *Cinchona succirubra* or *Cinchona robusta*. In mild benign tertian or quartan forms quinine sulphate or hydrochloride, ten grains three times a day after food, causes cessation of the fever. After this, 15 to 20 grains daily should be continued for one week, and after a week's interval repeated for another week to tide over the most likely time for relapse. In the case of malignant tertian fever quinine given intravenously (seven to ten grains in at least twenty cubic centimetres of sterile water or saline solution) has produced almost miraculous results. "Atebrin" or the soluble "Atebrin musonate" may be used instead of quinine during the febrile stage. It has the disadvantage of being toxic when combined with quinine, sometimes causes a yellow discoloration of the skin, and mental symptoms also. "Atebrin" is of service when quinine is contraindicated, for example, during pregnancy and in cases of blackwater fever, where quinine would aggravate the hemoglobinuria. During fever "Atebrin" is given in doses of 0.1 gramme three times per day for one week. The most

important diminution of relapses in malaria has resulted from the use of "Plasmoquine". In doses of 0.01 gramme three times per day for ten days it is effective in destroying the gametocyte stage and rendering the patient non-infective.

NEUROLOGY AND PSYCHIATRY.

The Incidence of Conjugal Neurosyphilis.

E. L. HUTTON (*The Journal of Mental Science*, July, 1941) sets out details of an investigation undertaken at the Horton Malaria Therapy Centre into the question of conjugal neurosyphilis. The material is based on the conjugal partners of female paralytics treated by malaria between 1925 and 1939, all congenital neurosyphilis being excluded. The conjugal histories of 492 female neurosyphilitics were studied. Tertiary syphilis was found to be rare in the infected partners of these women, while the incidence of neurosyphilis was unusually high. Such a finding, in the author's view, gives support to the theory of a neurotropic strain of spirochete. It was found that the contagious period of syphilis is short: if a man acquired syphilis, the contagious period rarely exceeded two years; in women the contagious period was from one to two years. The incidence of conjugal neurosyphilis was sufficiently high to warrant the adoption of routine measures for the diagnosis and treatment of all conjugal partners.

Convulsion Therapy in War Psychoneurotics.

RANKINE GOOD (*The Journal of Mental Science*, July, 1941) has studied 40 military psychoneurotics ranging in age from eighteen to forty-two years. All were in good physical health. Twenty-three had been engaged in actual fighting or had been subjected to such enemy action as machine-gunning, bombing or shell fire. For descriptive purposes they were divided into groups—eighteen cases of hysteria, four cases of anxiety neuroses, seven cases of cyclothymia, eight schizoid types and three psychopaths. No difference was noticed between psychoneurotics and psychotics in their attitude to the treatment, nor during the convulsion itself. The author claims that all patients but one showed varying measures of improvement as the result of treatment; but the ultimate prognosis as regards return to duty was poor. In his opinion this was not due to the inefficiency of the treatment, but to the negative therapeutic attitude of the patient.

The Aetiology of the Fugue States.

In a search for the common aetiological features in the fugue states E. Stengel (*The Journal of Mental Science*, October, 1941) presents 25 case histories, 18 of the patients being females. He found a relationship to epilepsy in 10 instances; one patient was a schizophrenic and the remaining 14 were typical manic-depressives, hysterics and psychopaths. Periodical changes of mood characterized the previous history of the majority of the patients studied. A further feature, considered by the author to have a definite relation to the development of fugue states, was some disturbance in the environmental conditions in childhood—some serious break in the child-parent relationship. In the greater

proportion of these cases the disrupted relationship occurred between the child and its parent of the opposite sex. Prolonged absence of one or other parent from home during the early childhood of the patient was found to play an important part in the aetiology of compulsive wandering; and such wandering is often stamped with the characteristics of a symbolic act. The onset of the fugue state was in females frequently related to menstruation; and the restlessness which was found to precede the development of the fugue was found to coincide with the premenstrual state. Sexual irregularities were often associated with fugue states: homosexual features were manifest in those who did not display them when not in the fugue state. Emotional traumata often seemed to precede the first fugue; and habitual emotional instability was a prominent feature in the previous history of many patients. The author believes that there are three conditions essential to the production of fugue states: periodic changes of mood, disturbances in the domestic relationship with the parents, and a tendency to day-dreaming and the production of twilight states. The author finally draws attention to problems arising out of war conditions, such as the breaking up of family life due to evacuation, and the possible psychological factors at work in desertion from military service.

Music, an Aid in Management of the Psychotic Patient.

THE therapeutic introduction of music by Ira M. Altshuler and Bessey H. Shebesta (*The Journal of Nervous and Mental Disease*, August, 1941) into hospital routine was prompted by desire to quieten disturbed mental patients. It was used alone and in conjunction with hydrotherapy. Noisy, inaccessible and chronic psychotic patients were chosen for observation; and music was found to be quite useful as a calming agent. It is suggested that the playing of familiar tunes brings back memories and recollections of reality which are desirable substitutes for phantasies, fear and excitement. Patients whose utterances were usually incoherent often joined in the singing of popular songs. Some fell into quiet sleep after listening to music for half an hour or so. Many expressed their appreciation and looked forward to further musical sessions. The authors suggest further and more extensive use of the controlled use of music.

Cutaneous Naevus with Buphthalmos and Epilepsy.

A DETAILED case report of Sturge's syndrome is contributed by Redvers Ironside and Denis Hill (*The Journal of Mental Science*, October, 1941). The patient was a soldier, aged twenty-six years, who was sent to hospital on account of repeated fits. It was found that the naevus flammeus was of unusually widespread distribution. Involving the right trigeminal area, the trunk and upper limbs, and the third division of the left trigeminal nerve. Glaucoma of the right eye was thought to be due to some vascular abnormality of the ciliary body or choroid. The fits were Jacksonian and contralateral. They resembled migrainous attacks, being preceded by telchopsia. The patient was of low mentality, having an intelligence quotient of 72. No calcification of the cerebral sulci was apparent in the X-ray picture. There was no abnormality in the cerebrospinal fluid; nor was any abnormality

revealed by electro-encephalography. The nature of the intracranial lesion could only be assumed.

The Allergic Factor in Idiopathic Epilepsy.

THE literature on allergy and epilepsy is passed in brief review by D. C. Dewar (*The Journal of Mental Science*, October, 1941) before he embarks on an investigation as to the allergic sensitivity of twelve epileptic patients. Nine of these patients had their symptoms alleviated by elimination and desensitization. A special skin testing technique is described. The author is of opinion that epileptics exhibit an allergic phenomenon common to them as a group, though he does not suggest that their convulsions arise from this hypersensitiveness alone. The desensitization was carried out by specific intramuscular injections. Dosage was controlled by reference to variations in the eosinophile cells in the differential cell count. The author believes that the question of allergy opens a wide field for further study in regard to epilepsy; the possibility of specific sensitivity should not be ignored in idiopathic cases; and the institution of treatment along the lines he has indicated may be undertaken not only for young patients with fresh illnesses, but for those whose illness has become chronic.

Scheid's Cyanotic Syndrome.

H. A. PALMER (*The Journal of Mental Science*, October, 1941) discusses the work of Scheid, whose syndrome embraced the triad of fever, cyanosis without dyspnoea and tachycardia, occurring in a schizophrenic setting. Apparently the syndrome may be subdivided into a haemorrhagic and non-haemorrhagic variety. They may be febrile, cyanotic episodes, ending fatally; certain non-fatal episodic febrile schizophrenias; and intercurrent febrile cyanotic episodes occurring in certain schizophrenic patients. The author describes a male patient, aged twenty, who was admitted to hospital three weeks after the sudden death of his brother. He was then in a confused, autistic schizophrenic state, with raised temperature, cyanosis and tachycardia. The temperature subsided, but the cyanosis and tachycardia increased. The mental condition deteriorated and he passed into a comatose condition and died. An autopsy revealed marked meningeal congestion, but no other cerebral abnormality. The liver showed intense fatty changes with secondary leucocytic infiltration.

The Effect of Menstruation on Seizure Incidence.

In an attempt to settle the question of the effects of menstruation in female epileptics Willard W. Dickerson (*The Journal of Nervous and Mental Disease*, August, 1941) studied the behaviour of 269 female epileptic patients for one year. He noted that the first epileptic attack often coincided with the onset of menstruation. In only 10% of his patients did he find a direct relationship between the seizure incidence and the menstrual period. In this group a relationship exists both in the number of patients experiencing seizures and in the number of seizures per patient. Of the patients, 12.3% had no seizures whatever during the period; and in the remaining 79.4% of the cases no regular relationship in seizure incidence could be demonstrated.

British Medical Association News.

SCIENTIFIC.

A MEETING of the South Australian Branch of the British Medical Association was held on November 27, 1941, Dr. R. J. VESCO, the President, in the chair. The meeting took the form of a number of clinical demonstrations by members of the Branch.

Rat-Bite Fever.

Dr. BRUCE LAWRENCE showed a male patient, aged thirty years, a baker by trade. Dr. Lawrence said that the man had suffered from an unusual type of pyrexia, which he considered showed sufficient features of the disease to justify a diagnosis of rat-bite fever. The man had sustained a wound on a finger whilst handling bags of flour which had been contaminated by rats. The wound had subsequently become swollen and reddened and axillary adenitis had developed. The illness had had an abrupt onset twenty-two days after the wound had been sustained, with a shivering attack, vomiting, headache and some giddiness, followed by fever. An erythematous rash had appeared on the third day, which became purplish and took the form of blotches. The legs became painful. Hyperæsthesia and paræsthesia developed, chiefly in the legs, and intermittent rises in temperature occurred. The temperature rose sharply to 101° or 103° F. and fell by crisis, usually within twenty-four hours from start to finish; the rises in temperature were accompanied by shivering or a feeling of shakiness, and by the appearance of one or two erythematous blotches, which faded with the fall of temperature. Between attacks the patient felt perfectly well and his temperature remained normal. The afebrile periods lasted for two days, the periodicity averaging fifty-two hours. The patient had lost two and a half stone in weight in five weeks.

Examination of the blood revealed that the leucocytes numbered 17,000 per cubic millimetre. No organism was grown on attempted culture from the blood, and dark-ground illumination gave negative results. An attempt to develop the infecting organism through a laboratory animal was spoilt through a misunderstanding.

The intravenous administration of neosarsphenamine was rewarded by immediate improvement in the patient's condition; the rises of temperature were delayed and were smaller than before, and after the third injection no further rise of temperature occurred. The patient felt and appeared completely cured.

Lupus Erythematosus.

Dr. L. W. LINN showed a female patient, aged fifty-eight years, on whose face a rash had first appeared in March, 1941. At first she thought it was due to sunburn; but instead of clearing up, it continued to extend and new lesions developed. The condition had been constantly present since the onset. The patient sunburned easily, but usually the burn healed quickly.

On examination several scaly, erythematous patches of varying size were present, mainly on the centre of the face. The scales were adherent, and when they were removed the typical horny plugs which had been penetrating the follicles were found. Dr. J. L. Hayward had made an exhaustive general examination of the patient, but no toxic focus was discovered and there was no evidence of any other gross abnormality. She had only recently come under observation and treatment had not yet been begun.

Dr. J. L. HAYWARD said that Dr. Linn had asked him to investigate the possibility of an associated chronic infective focus. Despite some slight symptoms of possible gall-bladder or urinary tract infection, investigation revealed no abnormality. There was some evidence that the patient was "subthyroid", and in this connexion it was interesting to note that Sir Trent de Crespigny had treated the patient twenty years earlier with thyroid extract. Dr. Hayward thought that the exhibition of thyroid extract in small doses was indicated again.

Dr. W. GILFILLAN showed a female patient, aged forty-two years, who had for five years had a patch of *lupus erythematosus* of the chronic discoid type on her scalp. The centre of the patch was characterized by atrophy and destruction of the hair follicles; it was surrounded by a spreading scaling erythematous margin. Three smaller patches had also been present for six months; they presented no obvious central atrophy.

Discussing the differential diagnosis, Dr. Gilfillan said that the condition was not *alopecia areata*, because of the absence of hair stumps in the form of exclamation marks

and the presence of atrophy. Psoriasis could be ruled out because of the absence of silvery scales and the destruction of hair follicles. A syphilitic origin for the condition seemed to be denied by the fact that the patient's blood serum failed to react to the Wassermann test. With regard to prognosis, Dr. Gilfillan said that the patient was in good health and no focus of infection could be found. In her case there was not the same risk of an acute flare-up of the condition into acute disseminated *lupus erythematosus*, as in the case of the patient suffering from subacute disseminated *lupus erythematosus* shown by Dr. Linn. Treatment would consist in the administration of quinine or sodium salicylate by mouth and of bismuth or gold salts by injection. Sulphanilamide had given good results in some cases.

Colloid Degeneration of the Skin.

Dr. Linn also showed a male patient, a police constable, aged forty-four years, who about seven years earlier had noticed a roughness on the backs of his hands. The condition gradually spread and became thicker, and about three years ago it had spread to his face. The eruption looked like a collection of blisters, which bled easily when knocked or scratched; no irritation or discomfort was present. The condition was always worse in summer. The patient's general health was good. He had been on point duty for eighteen years, and before that he had been exposed to the sun a great deal, farming and working as a wharf labourer.

On examination the backs of his hands were seen to be covered with hundreds of small dome-shaped or quadrilateral tumours. The lesions were closely set but discrete; they were yellowish or pale brown in colour and had a peculiar translucent appearance. They looked and felt like flat-topped tense vesicles, but when they were pricked only a small amount of gelatinous fluid escaped. For the last six months the patient had been protecting his hands from exposure to the sun and the eruption had subsided considerably.

Dr. Linn remarked that the two patients he had shown provided examples of lesions in which exposure to sunlight had been a prominent factor as a causative agent.

Toxic Erythema.

Dr. Gilfillan also showed a female patient, aged fifty-five years, who in the past twelve months had had three attacks of sore throat and malaise followed by toxic erythema of the *erythema multiforme* class. In the present attack a variety of lesions were present; erythematous macules and plaques, some having gone on to form vesicles, affected the exposed areas. The patient's tonsils were enlarged, and Dr. Gilfillan considered that the attacks would continue until they were removed. Treatment would consist in the oral administration of acetylsalicylic acid or sulphanilamide and the local application of soothing substances, such as hot calamine lotion or zinc cream. The source of the toxæmia was to be sought and removed if possible.

Addison's Disease.

Dr. G. A. LENDON showed a patient suffering from Addison's disease, who had been treated with grafts of suprarenal gland. Though the patient's sodium balance had been satisfactorily stabilized by means of cortical extract, yet the difficulty of continuing the treatment away from town led to an attempt to establish a satisfactory graft. Two intrasternal grafts had been prepared and introduced by Dr. Thiersch. The first was from a four months' fetus, and it brought about a considerable reduction in the amount of cortin necessary to maintain an adequate sodium balance; but no improvement resulted from the second graft, probably because the fetus was later found to have been dead for twelve hours when the suprarenal glands were removed. It was proposed to attempt a third graft when material became available.

Dr. Lendon said that in another case the sodium balance had been maintained for four months after the grafting without the use of cortical extract. To illustrate the degree of improvement, he quoted the blood pressure figures: with the combined use of cortical extract and a graft the systolic pressure had risen from 75 to 145 millimetres of mercury and the diastolic from 50 to 90. Salt had become distasteful to the patient.

Paralysis of the Right Side of the Face.

Dr. H. M. JAY showed a male patient who had been referred to him in September, 1935, with a history of right-sided facial paralysis of nine weeks' duration. The paralysis was of the lower motor neurone type and was associated with chronic suppurative otitis and an extensive cholesteatoma. A radical operation on the mastoid was performed, and subsequently it became necessary to destroy the labyrinth on account of severe and persistent vertigo. At the same

time 10 millimetres of the facial nerve, which represented the damaged portion, were resected, and a graft from the superficial cerebral nerve was inserted fourteen days later in the manner of Ballance and Duell. Massage and electrical treatment were instituted, and a hook was worn to elevate the angle of the mouth. After six months of treatment the patient disappeared and was not seen again until a few weeks before the meeting, when he reported at the outpatient department and said that he could now move the right side of his face. Dr. Jay demonstrated movements of the muscles that had received support from the hook during the past six years, but pointed out that return of function in the upper part of the facial musculature was unlikely now, owing to stretching and fibrosing of the muscles. He stressed the fact that such patients had to be watched over a long period if good results were to be obtained.

Public Health.

THE STERILIZATION OF SURGICAL CATGUT.

THE following notes on the question of the sterilization of catgut have been received from the Director-General of Health, Commonwealth Department of Health, Dr. J. H. L. Cumpston.

The information was compiled by Dr. R. E. Richards, of the Department of Health, for the twelfth session of the National Health and Medical Research Council, which met in Canberra on November 26 and 27, 1941, and adopted the following resolution in this connexion:

The Council, having heard the report upon the sterilization of catgut, resolves that the report be printed as an appendix to the report of this session and that copies be sent for publication also to THE MEDICAL JOURNAL OF AUSTRALIA and made available on application to hospital authorities and hospital journals.

This action originated from a request from Sir Raphael Cilento that the matter of surgical catgut might well be brought before the National Health and Medical Research Council to determine whether or not there should be: (i) regulations to control the preparation and sale of surgical catgut; (ii) a pamphlet or some such publication or a note to THE MEDICAL JOURNAL OF AUSTRALIA upon the status of catgut.

This request had arisen owing to a series of wound infections in Queensland, which were reported to have been caused by catgut sold in ampoules already "sterilized" by a chemical process.

In three of these cases the infection was by tetanus.

Cilento also supplied the following information:

Brewer, acting for the Council of Pharmacy and Chemistry of the American Medical Association (see J.A.M.A., 27th February, 1937, page 722) concludes that no chemical method of sterilizing catgut is reliable, and that heat sterilization is the only satisfactory method. In consequence of this report, the leading firms in U.S.A. preparing catgut have all adopted heat sterilization.

Some leading surgeons in Brisbane and elsewhere have practically given up the use of catgut. Apart from the uncertainty as to its sterility, catgut is more irritant to tissues than cotton or silk.

The following questions arise:

1. Should the use of catgut be completely abandoned? Further opinions from surgeons would be needed on this aspect.

2. Should the sale of chemically "sterilized" catgut for surgical use be prohibited?

3. Should the practice of hospitals of "sterilizing" catgut by chemical methods for their own use be prohibited?

4. Should practitioners be informed by circular of the exact status of catgut sutures after an investigation has been made?

These four proposals were submitted on 19th December, 1940, to the British Medical Association (Queensland Branch), and on 29th July, 1941, a reply was received to the effect that a joint committee of the British Medical Association and the Royal Australasian College of Surgeons had dealt with the matter and had recommended as follows:

1. The use of catgut cannot be completely abandoned because the use of absorbable sutures is almost essential in certain situations. A much more extensive use of silk and particularly of cotton is desirable because (a) they are less irritating to the tissues; (b) they can be sterilized with certainty by heat; (c) in the case of cotton, its tensile strength increases on exposure to moisture, as during boiling, and on implantation of tissues; (d) they are immeasurably cheaper. As an example of this, a surgeon writing in the *Annals of Surgery*, May, 1941, states that by the use of cotton instead of catgut he has reduced his hospital suture bill for eight months from 15.00 dollars to 4 dollars 20 cents.

2. The catgut prepared by commercial firms should be allowed for sale only when approved methods of sterilization and approved safeguards are used, which should be clearly stated in relation to its sale.

3. As regards the chemical preparation of catgut by individual hospitals, this should only be permitted when adequate safeguards for its sterilization are practised, such as bacteriological testing and approved methods of sterilization are used. In this connexion the mercurial method of sterilization is certainly not adequate and should be abandoned.

4. We agree that the results of an adequate research into the present status of catgut should be made available for the profession.

The Medical Research Council of the Privy Council in 1929 issued in its Special Report Series Number 138 a comprehensive report by Bulloch, Lampitt and Bushell dealing with the preparation of catgut and methods for its sterilization.

The following data have been abstracted from this report:

Historical.—The modern catgut period really started with a paper by Joseph Lister (1869), "Observations on Ligature of Arteries in the Antiseptic System". Lister had been using a silk ligature steeped in watery solution of carbolic acid and found in one instance during a *post mortem* of a person who had died one month after the operation that the knot and ends of the silk ligature were lying in a small cavity which contained a liquid apparently purulent.

As Lister had implicit faith in the antiseptic action of the carbolic acid used, he concluded that the purulent collection was caused by some irritant action of the silk itself and then decided to use catgut as a substitute for silk.

The use of animal ligatures had been previously employed, but never had they been exposed to an antiseptic.

He used at first the watery solution of carbolic acid, but subsequently used carbolic acid in olive oil in an endeavour to achieve a ligature which was sterile, supple, strong and absorbable.

In 1881 Lister believed he had effected a definite improvement in the preparation of the catgut by the use of a mixture of chromic acid and carbolic acid.

In the same year Koch published his classical experiments on disinfection, and among other revelations he clearly showed that a saturated solution of carbolic acid, on which Lister had placed such reliance, could not kill anthrax spores in three months, and that the carbolic and olive oil mixture was devoid of any antiseptic action whatsoever.

Following the fall of carbolic acid from the pinnacle, there was the corrosive sublimate period. This lasted until about 1903. In the meantime the use of formalin was becoming popular, but apparently died out completely in 1909.

Then there was the aseptic period, where the sterilization was by heat instead of chemicals.

Sterilization by Heat.—As the presence of water in a medium for transmitting heat to catgut has a deleterious effect on its physical properties, various anhydrous fluids were tried.

Some of these fluids possessed in themselves definite antiseptic powers, but for others no such claims could be advanced, and in such cases the sterilization is brought about by heat alone. Included in these anhydrous fluids tested were alcohol, ether, chloroform, acetone, benzene, toluol, xylol, anilin, vegetable oils, paraffin, cumol and hot air. This period lasted until 1907.

Iodine.—Then there came the iodine period, inaugurated by Claudius in 1902 and lasting to the present time in many variations.

Bulloch states that he has made many hundreds of experiments in the disinfecting action of iodine and can confirm the claims of Claudius that a 1% aqueous solution of iodine and potassium iodide applied for eight days (not less) will sterilize the most contaminated catgut almost infallibly.

He adds that iodine is practically the only substance by which a chemical sterilization of catgut can be obtained on a commercial scale.

The only disadvantage of iodine sterilization of catgut is the deterioration which takes place in the tensile strength when the ligatures are kept for a prolonged period in the solution. Methods have been since devised whereby this deterioration has been largely overcome.

Hydrogen Peroxide.—Hydrogen peroxide was claimed by Goris to be of great value in the manufacture of catgut. These claims were confirmed by Bulloch, who investigated various strengths at different pH values.

This method is of particular value in treating the ribbons prior to their being twisted into catgut.

Summary.—At this stage of the report the investigations into the methods of sterilization were summarized on these lines.

From a commercial point of view, the preparation of catgut on a big scale resolves itself into chemical sterilization by iodine and peroxide of hydrogen, or the physical sterilization by heat.

That catgut can be efficiently sterilized is not in question, but sterilization is only one problem that the catgut manufacturer has to contend with, for in addition to being sterile, the tensile strength and flexibility must not be injured.

Bacteria in Catgut.—The presence of bacteria in catgut was first noted in 1879, and in 1890 Brunner made an important contribution to the bacteriology of catgut in isolating and describing a bacillus, now considered to be the *Bacillus mesentericus ruber*, the spores of which are particularly resistant to sterilization. The presence of this organism in sterilized catgut has been noted up to the present time.

Other common contaminants were the spores of *B. subtilis* and the non-sporing microbes, such as *Micrococcus tetragenus*.

As a result of animal experiments, observers were of the opinion that the *Bacillus mesentericus ruber* in pure culture was non-pathogenic, but in the presence of other organisms, such as a harmless type of streptococcus, had an exalting action on the virulence of the streptococcus with resulting sepsis.

Catgut Infections in Man.—From the advent of catgut for surgical purposes until the present time infections alleged to be caused by its use have been a constantly recurring theme in surgical literature.

Bulloch considered that when this literature is examined critically little of it will be found to bear scrutiny, and gives a number of instances where there was no scientific confirmation whatsoever to show that the catgut was necessarily to blame. Of particular interest is the chapter dealing with the alleged connexion between catgut and post-operative tetanus. Richardson (1909) collected notes of 21 cases of tetanus after operation; 18 terminated fatally. Catgut had been used in all. In 14 the catgut was examined, and in four a bacillus resembling tetanus was found, but in no case was it tetanogenic.

In addition, medical literature contains quite a number of cases of post-operative tetanus in which no catgut was used.

Post-operative tetanus would appear to be a very unusual complication, as shown by figures from the London Hospital for the period 1906-1926.

During this period there were 111,519 major operations and there were only two cases of post-operative tetanus.

Bulloch, in commenting on this complication, concludes: "From a critical survey of most of the literature on post-operative tetanus it appears that, although there may be a suspicion against catgut, it remains for the most part only a suspicion." In almost all the cases of "catgut" tetanus, there have been other sources of infection which have either been left unconsidered or have not been adequately differentiated before the diagnosis of catgut tetanus was made.

Tetanus Carriers.—Included in various investigations into the incidence of tetanus carriers in human beings is one carried out by Bauer and Meyer (1926), who found 120 instances (24.6%) of tetanus bacilli in the faeces of 487 persons examined from various counties in the vicinity of San Francisco.

The sex distribution was practically equal, and occupation appeared to play no important role in the distribution of the carriers, whose age varied from $3\frac{1}{2}$ to 80 years.

The literature on the incidence of tetanus bacilli in the intestine of the sheep is exceedingly meagre, and only one paper on this subject was found, namely, that by A. Hoffmann (1905). Hoffmann examined the faeces of the guinea-pig, rabbit, sheep, cattle and horses.

Mice were injected with anaerobic cultures of the faeces and in 22 experiments he succeeded in reproducing tetanus only once, and that was by injection of the filtrate from a horse faeces culture.

The Present Position in Australia.

The following information deals with the position, as it stands at present, of the measures used for sterilization of catgut by heat in Australia.

The Military Board insist upon the following conditions in relation to Army supplies of catgut:

1. It shall be sterilized by heat.
2. Of each batch supplied, 1% shall be tested for sterility by an external authority, which shall be a bacteriological department of a university or of an institute attached to a teaching hospital of a medical school. The certified result of this test must be supplied to the inspecting officer.
3. The method for carrying out sterility tests shall be as described by R. O. Clock in *Surgery, Gynecology and Obstetrics*, 1935, LXI, 789. An additional step is demanded, namely, that before proceeding with these tests the gut shall be immersed for twenty-four hours at room temperature in absolute alcohol which has been sterilized by filtration.
4. All outer packages shall be intelligibly marked with the date of packing.

The Board supplied the following additional information: The method of sterilization used by the manufacturers is that of heating in fluids, such as kerosene, toluol, xylol, cumol or perchlorethylene. The temperature used lies between 150° C. and 165° C. By ensuring that the temperature of 160° C. is maintained for a recommended period of two and a half hours the tests of sterility show less than 2% non-sterile samples. A lower temperature produces less satisfactory figures.

Dr. T. H. Small, in an article in *THE MEDICAL JOURNAL OF AUSTRALIA*, October 11, 1941, describes a method using perchlorethylene as the medium in which the gut is heated for sterilization. Perchlorethylene is a fluid having a boiling point of 119° C., it is soluble in alcohol and evaporates at room temperature, and is not an antiseptic, so does not interfere with sterility tests.

The contaminant used in his tests was *Bacillus subtilis*, the spores of which will resist boiling in water for hours as against those of *Bacillus anthracis*, which are killed in ten minutes.

He later found, however, that a certain strain of *Bacillus mesentericus* was more resistant to sterilization than the *Bacillus subtilis*, but that catgut infected in this organism could be sterilized when heated in perchlorethylene at 160° C. at 25 pounds pressure for four hours. Biological tests, with catgut so treated, in regard to breaking strength, absorption time and tissue reaction are claimed to be quite satisfactory.

Laboratory Report.—A report from one of the laboratories carrying out the sterility tests for the Army contained the following information:

It was found that when the temperature for heat sterilization was raised from 150° C. to 160° C. the incidence of non-sterile tubes was greatly reduced.

The organisms most commonly found in the contaminated gut are of the mesentericus and pseudo-anthrax type.

A surgeon who had been having trouble with breaking down of wounds when using heat-sterilized catgut finally overcame this difficulty by using London Hospital catgut, which is sterilized by the iodine process.

The organisms found were considered to be non-pathogenic, but have proteolytic properties which would probably have something to do with the breaking down of wounds.

The manager of one of the three main surgical catgut manufacturing firms supplied information relating to his firm's methods of sterilization, and the following abstracts are of interest:

Last year our catgut was tested for sterility in the Walter and Eliza Hall Institute, Melbourne, according to Clock's method, and some tubes grew sporing organisms of the mesentericus type. Similar results were reported by Professor Ward, of Sydney University. I had the opportunity to discuss the whole problem with Colonel Kellaway and also with Professor Ward, and following their suggestion I increased the temperature and sterilized at 158° C. (20 lbs. pressure) for one hour. Professor Ward reported sterility after two weeks' incubation; however, during the third or fourth week a few tubes produced growth of *B. mesentericus*. I then sterilized at 160° C. (25 lbs. pressure) for 2½ hours, and now Professor Ward found all tubes sterile. Further tests were carried out at the Walter and Eliza

Hall Institute, Melbourne. Altogether 108 tubes were tested, but because I was afraid that this high temperature might interfere with the tensile strength I submitted 48 tubes sterilized at 160° C. for 2½ hours, and 60 tubes sterilized at 158° C. for 4 hours. All tubes were found to be sterile. Apparently a longer time at a slightly lower temperature had the same effect as a higher temperature for a shorter time. We are now sterilizing at 158° C. (20 lbs. pressure) for 4 hours.

As regards organisms found in Australian catgut, I should like to point out that our gut material is treated in its ribbon state before spinning (after removal of the mucous membrane) twice for 24 hours with 3 vol. % hydrogen peroxide. The original bacterial flora of the gut material is thus completely destroyed. (Bullock has reported that he has "treated infected ligatures with 3 vol. % H₂O₂ for 2, 3, 4, 5½ and 8 hours. All ligatures were found to be sterile; controls yielded stinking growths".) However, the ribbons are infected again when they are washed and spun; the raw ligatures are handled a good deal when they are sandpapered and polished, graded and wound on reels. Organisms found in our catgut before or after sterilization, therefore, are due to secondary infection and must be of the type found anywhere and everywhere.

Summary.

It would appear that catgut can be effectively sterilized. The iodine method as practised by the London Hospital seems to give the most consistent results as to sterility tests of the marketed product.

The sterilization by heat seems to have the disadvantage of the chance of contamination after sterilization during the bottling process, there being no antiseptic present to combat such contamination. Similar difficulties are experienced in bottling human serum; this has been largely overcome by the use of special rooms with filtered air *et cetera*.

In the storing of catgut in alcohol the pH value of the fluid is most important, namely, catgut will soon lose in breaking strength if stored in alcohol with a pH below 7.0. If the pH value is 7.6, this property is practically unaffected. Alcohol of pH 7.6, however, when used for this purpose, will gradually drop to pH 7.0 in about 12 months.

Bullock and others have shown that biniodide of mercury, even in concentrations up to 8%, is absolutely useless.

The common contaminants found in the sterility tests, *viz.*, organisms of the mesentericus and pseudo-anthrax types, are probably non-pathogenic, but may have a proteolytic action.

It is possible that the contamination by these organisms happens after sterilization.

The chance that catgut, sterilized under the above conditions, should harbour tetanus organisms is very remote.

The further question of the manufacture and sterilization of catgut in Australia was considered by the Federal Health Council in 1936, when the following resolution was passed:

This Council requests the Commonwealth Serum Laboratories to investigate the practicability of manufacturing catgut in Australia.

As a result of this investigation, it was decided that no further action be taken, as there were certain technical difficulties.

The control of the manufacture of catgut by the Commonwealth Government is limited and can only be applied to products manufactured for export, and, in addition, details of manufacture cannot be laid down. In the Therapeutic Substance Regulations—not to be enforced until after the war—it is laid down that catgut shall be sterile, but the methods of producing sterility are left in the hands of the manufacturers. At the present time regulations specifying methods of manufacture and producing sterility are purely a matter for the States.

Medical Practice.

THE REGISTRATION OF ALIEN DOCTORS.

The following National Security (Alien Doctors) Regulations were notified in the *Commonwealth of Australia Gazette* of February 11, 1942.

1. These Regulations may be cited as the National Security (Alien Doctors) Regulations.

2. These Regulations shall be administered by the Minister of State for Health.

3. In these Regulations, unless the contrary intention appears:

"applicant" means an applicant for a licence under these Regulations;

"approved" means approved by the Board;

"Committee" means an Examining Medical Committee established in pursuance of regulation 5 of these Regulations;

"licence" means a licence issued under these Regulations;

"the Board" means the Commonwealth Alien Doctors Board established in pursuance of regulation 4 of these Regulations.

4. There shall be a Commonwealth Alien Doctors Board consisting of the Commonwealth Director-General of Health, who shall be the Chairman of the Board, and two other members who shall be appointed by the Minister.

5. (1) There shall be an Examining Medical Committee in each of the States of New South Wales, Victoria, Queensland and South Australia, consisting of—

The Professor of Medical Jurisprudence, who shall be the Chairman of the Committee;

The Professor of Medicine;

The Professor of Surgery; and

The Professor of Obstetrics,

in the University in the State.

(2) If a University in any State has no officer holding any of the titles referred to in the last preceding sub-regulation or, in the event of the illness of any of these officers, the Minister may appoint another officer of that University to be a member of the Committee in that State, who, in the opinion of the Minister, has, for the purposes of these Regulations, an equivalent status.

6. There shall be payable to each member of the Board or of a Committee fees and allowances at such rates as the Minister determines.

7. (1) Any person who is, by the law of any country outside Australia, qualified to practise medicine in that country, may apply in accordance with the approved form to the Chairman of the Board for a licence under these Regulations.

(2) The applicant shall—

(a) set out in his application the name by which he was ordinarily known before his arrival in Australia;

(b) supply original diplomas, certificates, testimonials or licences, or other documents, in support of his application; and

(c) supply such other information as the Board or a Committee requires.

8. (1) Any person making application for a licence shall attend for examination at the time and place notified to him by the Chairman of the Board or of a Committee.

(2) The applicant may be required to answer any questions either orally or in writing, which may be put to him by either the Board or a Committee.

9. A Committee shall report to the Board in accordance with the approved form whether, in its opinion, any applicant examined by it—

(a) has a knowledge of the English language adequate for the conduct of medical practice;

(b) possesses the requisite knowledge and skill for the efficient practice of medicine, surgery and obstetrics according to the standards in force at any Australian University;

(c) possesses the requisite knowledge and skill for the efficient practice, as a specialist, of one of the special branches of medical science.

10. (1) After consideration of any report from a Committee in respect of any applicant, the Board may grant, or may refuse to grant, a licence to the applicant.

(2) A licence granted under this regulation may be—

(a) a licence to practise medicine in all branches of medical science; or

(b) a licence to practise medicine in one or more branches of medical science specified in the licence.

(3) Any such licence may be unlimited as to place or area or may be limited as to any institution, service or area within the Commonwealth specified in the licence.

(4) Subject to these Regulations any such licence shall be valid for such period as is specified in the licence.

(5) In addition to any limitations to which any such licence is subject in accordance with the foregoing provisions of this regulation the licence may be subject to such qualifications or conditions as are specified in the licence.

11. A licence shall be in accordance with the approved form.

12. (1) The Board may, in its discretion, cancel any licence or may suspend any licence for such period as is determined by the Board.

(2) Any person whose licence is so suspended or cancelled may appeal to the Minister, whose decision on the appeal shall be final.

13. Notwithstanding anything in the law in force in any State, any person licensed under these Regulations shall be entitled to practise medicine in any such State, subject to the limitations, conditions or qualifications specified in his licence.

14. Any person licensed under these Regulations shall, if so required by the Minister, practise medicine in any locality or place, and under such conditions (if any) as the Minister directs.

15. Notwithstanding anything in these Regulations, every licence shall lapse and be no longer valid on the day on which the *National Security Act 1939-1940* ceases to be in force.

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 45, of February 12, 1942.

AUSTRALIAN MILITARY FORCES.

AUSTRALIAN ARMY MEDICAL CORPS.

Seventh Military District.

Captain (provisionally) N280187 J. F. Ireland is transferred from Australian Army Medical Corps, 2nd Military District, 19th December, 1941.

Eighth Military District.

Lieutenant-Colonel E. T. Brennan, D.S.O., M.C., is appointed from the Reserve of Officers, 23rd December, 1941.

Northern Command.

First Military District.

To be Lieutenant-Colonel (temporarily).—Captain (Temporary Major) J. A. McGree, 20th December, 1941.

To be Majors (temporarily).—Captains (provisionally) W. V. Connor, T. R. Biggs, L. Morris and A. Inglis, 12th January, 1942.

To be Honorary Captains.—Francis Rupert Benson, 7th January, 1942, and Charles Dight Barlow, 9th January, 1942.

Eastern Command.

Second Military District.

Captain (provisionally) (Temporary Major) W. T. J. Harris is transferred from Australian Army Medical Corps, 7th Military District, and retains the temporary rank of Major, 13th January, 1942.

Captain (Temporary Major) P. Gilbert relinquishes the temporary rank of Major and is transferred to the Reserve of Officers (A.A.M.C.), 16th December, 1941.

Honorary Captains H. C. Spencer and R. H. Kenny are appointed from the Reserve of Officers (A.A.M.C.) and to be Captains (provisionally), 24th December, 1941, and 3rd January, 1942, respectively.

To be Major (temporarily).—Captain N274194 E. S. Stuckey, 6th January, 1942.

To be Captain (provisionally).—Joseph Christie, 15th January, 1942.

The resignation of Honorary Captain R. G. Bligh of his commission is accepted, 25th December, 1941.

To be Honorary Captains.—John Ross, Thomas William Freeman, Patrick Edward McCormack, 9th January, 1942, Bernard Moreton Birkenhead Riley, 12th January, 1942, William Henry Cook, 13th January, 1942, and John Joseph Gard, 14th January, 1942.

Southern Command.

Third Military District.

To be Major (temporarily).—Captain (provisionally) V19645 R. B. Perrins, 6th January, 1942.

Honorary Captain C. W. Kingston is retired, 2nd February, 1942.

Fourth Military District.

Major F. L. Wall, M.C., is appointed to command a Casualty Clearing Station, 1st November, 1941, and to be Lieutenant-Colonel (temporarily), 1st January, 1942.

To be Lieutenant-Colonels (temporarily).—Major L. C. E. Lindon and Captain E. B. Jones, 5th January, 1942.

ROYAL AUSTRALIAN AIR FORCE.

Citizen Air Force: Medical Branch.

The following Flight Lieutenants are promoted to temporary Squadron Leaders, with effect from 1st January, 1942: R. W. D. Fisher, E. S. Peters, (Acting Squadron Leaders) L. J. T. Murphy, F. S. Parle, J. A. Game, A. W. Raymond, M.C., W. McL. Borland, W. M. Lemmon, J. C. Sangster, F. G. Steele, J. E. Jordan, K. K. Stringer, J. J. Arnold, M. J. H. Hutchison.

Flying Officer (Acting Flight Lieutenant) H. J. R. Gamble is promoted to temporary Flight Lieutenant, with effect from 1st January, 1942.—(Ex. Min. No. 34—Approved 4th February, 1942.)

The following Flight Lieutenants are granted the acting rank of Squadron Leader whilst employed as Squadron Leaders, with effect from 9th December, 1941: M. H. B. Robinson, G. J. B. Baldwin, F. R. Wicks.—(Ex. Min. No. 36—Approved 4th February, 1942.)

The following are appointed to commissions on probation with the rank of Flight Lieutenant, with effect from the dates indicated: Collin Campbell Greenwell, M.B., B.S., Otto Henry Schneider, M.B., B.S., 29th December, 1941; Edward Vanderbyl Waddy Pockley, M.B., B.S., D.O., D.O.M.S., F.R.A.C.S., 14th January, 1942; Harvard Northcroft Merrington, M.B., B.S., 15th January, 1942.

Robert Hiddlestone is appointed to a commission on probation with the rank of Pilot Officer, with effect from 5th January, 1942.

The following are transferred from the Reserve to the Active List, with effect from 5th January, 1942: Flight Lieutenants G. Matthews and R. G. Weaver.

Reserve: Medical Branch.

The following are appointed to commissions on probation, with the rank of Flight Lieutenant, with effect from the dates indicated: George Matthews, L.R.C.P., L.R.C.S., L.R.F.P. and S., C.M., Ph.D., Frederick George Middleton, M.B., B.S., 18th December, 1941; Richard Geoffrey Bligh, M.B., B.S., George Alfred Hodgson, M.B., B.S., 26th December, 1941.

Flight Lieutenant L. O. Morgan relinquishes his commission with effect from 16th December, 1941.—(Ex. Min. No. 33—Approved 4th February, 1942.)

The following are transferred from the Active List to the Reserve, with effect from 12th January, 1942: Flight Lieutenants R. M. Buntine, C. R. E. Downing, H. R. Hawkins.—(Ex. Min. No. 37—Approved 4th February, 1942.)

COURSE OF LECTURES IN BRISBANE.

THE Deputy Director of Medical Services, Northern Command, announces that a series of lectures on military medicine will be held on successive Tuesdays at the Physiology School, University of Queensland, William Street, Brisbane, at 8.15 o'clock p.m. The lectures will be open to officers of the Australian Army Medical Corps in the metropolitan area and to senior non-commissioned officers nominated by their commanding officers. The programme is as follows:

March 3, 1942.—"Wound Treatment in the Forward Area": (i) "At the R.A.P.", Lieutenant-Colonel J. J. Power, D.S.O.; (ii) "In the Field Ambulance", Captain A. E. Lee.

March 10, 1942.—"Treatment of Shock in the Field": (i) Captain A. E. Lee, (ii) Lieutenant-Colonel L. McKeon.

March 17, 1942.—(i) Demonstration of methods of blood grouping in the field, Major N. M. Gutteridge; (ii) "The Use of Service Transfusion Panniers", Captain R. S. Lahz.

March 24, 1942.—"Emergencies in Army Surgery": (i) Wing Commander N. G. Sutton, (ii) Lieutenant-Colonel L. McKeon.

March 31, 1942.—"Emergencies in Army Medicine": (i) Major A. P. Murphy, M.C., (ii) Group Captain S. F. McDonald.

April 7, 1942.—Lecturettes on treatment: (i) "Malaria", Lieutenant-Colonel Sir R. Cilento; (ii) "The Dysenteries", Lieutenant-Colonel Sir R. Cilento; (iii) "Scabies", Captain B. B. Barrack; (iv) "Tinea", Captain B. B. Barrack.

April 14, 1942.—"Preventive Medicine": (i) "Care of the Feet", Lieutenant-Colonel H. M. Saxby; (ii) "Avitaminoses", Major D. H. K. Lee; (iii) "Control of Venereal Disease", Squadron Leader V. N. B. Willis; (iv) "Heat Exhaustion", Major D. H. K. Lee.

April 21, 1942.—(i) "Closed Treatment of Wounds", Major A. V. Meehan; (ii) demonstration of plastic technique, Major G. A. Douglas, O.B.E.

CASUALTIES.

ACCORDING to the casualty list received on February 23, 1942, Captain J. F. Park, A.A.M.C., of Prahran, Victoria, is reported missing. Captain G. L. Lindon, A.A.M.C., of Toorak, Victoria, is reported killed in action, and Captain R. M. Mills, A.A.M.C., of Narrabeen, New South Wales, is reported wounded in action.

Correspondence.

SNAKE BITE AND PITUITRIN.

SIR: The recent fatal case of poisoning from a death adder bite, in Manly, made me wonder if by any chance my experience in the Northern Territory at Groote Eylandt would be of any value.

Death adders are frequently seen at Groote Eylandt during the wet season. The natives are terrified of them because the bite is always fatal to them and Groote is hundreds of miles from medical aid.

During one month I found I had to treat three cases of poisoning—a bite by snakes, since shown to be death adders, being the cause. In each case I gave pituitrin as soon as possible and repeated the dose in two to four hours. The usual snake bite treatment was given and the patient was wrapped in blankets, with hot-water bags, and given hot milk and brandy until the condition improved.

After three to four hours there was no distress in breathing and the pulse had picked up well.

After a few days the patients became quite normal.

Two children and one man were saved by pituitrin that month—the man was in a very collapsed condition, his pulse 20 and respiration very distressed—he had been given strychnine first. Then four hours later was given one cubic centimetre of pituitrin and four hours later a second injection, with the result that his life was saved.

Yours, etc.,

ELIZABETH TAYLOR.

"The Moorlands",
Mt. Colah,
Via Hornsby,
New South Wales.
January 15, 1942.

CYCLOPROPANE.

SIR: I wish to protest against the action of the Medical Supply Committee in relegating cyclopropanum to class "C".

It is obvious that the personnel of the Committee is unacquainted with the value of this anaesthetic agent.

Used in its proper sphere and with sound knowledge of its action, it is the nearest approach to the perfect anaesthetic yet available.

The fact that the possibilities of the drug have been explored by only a limited number of anaesthetists in Melbourne and that, therefore, its qualities and virtues are thoroughly known to a limited number of surgeons possibly accounts for this unfortunate classification.

One might reasonably ask if anyone competent to express an opinion was consulted before the Committee reached its decision.

I am certain that the anaesthetists in Perth, Sydney and Adelaide will support my request for a reclassification of this drug into class "A".

The annual consumption of cyclopropane is not large, and the small amount it will be necessary to import will impose no strain on shipping space.

Yours, etc.,

DOUGLAS G. RENTON, M.B., B.S., D.A.

12, Meadow Street,
East St. Kilda,
Victoria.

February 2, 1942.

IODOXYLUM AND "PERABRODIL".

SIR: According to the classified list of drugs issued by the Medical Equipment Control Committee and published in the journal of January 31, Iodoxylum, B.P., is identical with "Perabrodil". This is incorrect. The two drugs differ chemically and are not always interchangeable. Iodoxyyl is the disodium salt of 3:5-di-iodo-4-pyridoxyl-N-methyl-2:6-dicarboxylic acid. "Perabrodil" is the di-ethanolamine salt of 3:5-di-iodo-4-pyridone-N-acetate. "Perabrodil", which is now often used by subcutaneous and intramuscular injection, does not cause the severe tissue reaction which is brought about by extravasation in the case of Iodoxylum.

It has been announced in *The British Medical Journal* that the question of including "Perabrodil" in the British Pharmacopoeia under an official title is under consideration. This fact points to the desirability of avoiding confusion between the two preparations.

Yours, etc.,

C. W. ROBINSON, M.P.S. (Gt. Brit.).

60-66, Hunter Street,
Sydney.
Medical Department,
Bayer Pharma Pty. Ltd.

February 3, 1942.

INDUSTRIAL ACCIDENTS.

SIR: For twenty-two years I was Commonwealth Medical Officer at the General Post Office, Sydney, and saw numerous accidents and their after-results. There is no sadder thing than a crippled working man; not only is he unable to support his family—and those of us who work among them must recognize their honesty and their aim to keep their family well and to place their children in positions where they can earn a good living—but he can no longer pull his weight in the community.

Now that I have retired from practice I feel that I can write freely on this subject.

All serious accidents, for example, injuries to limbs and joints, should be put at once under the care of a trained orthopaedic surgeon and all means used to cure.

I have often visualized a big clinic under the charge of a highly skilled man, who would be paid a good salary, with an adequate staff, beds for in-patients, a gymnasium, workshops and a large staff of trained masseurs, so that early and proper treatment could be given to in- and out-patients.

Massage should be early and not left until the joint is stiff from long plaster treatment, and massage treatment should not be measured by the clock.

I can vouch from personal experience that after any operation massage makes you feel far better and stronger on discharge. The workshops are of especial value, as a man can be trained in a new trade if the injuries be so extensive as to prevent him going back to his former occupation—for example, a lineman with a fractured calcaneum or a strained knee joint, either of which would prevent him using a ladder or stirrups. A mechanic with a damaged hand: light work at the bench will cure stiff fingers far quicker than any other treatment, and the interest of working will have a profound mental effect.

At Southall, where we had a small workshop, the effect on the men employed there was very marked.

Yours, etc.,

A. H. MOSELEY.

Leaton,
Goonoo Goonoo Road,
Tamworth,
New South Wales.
February 7, 1942.

"DRIVING UNDER THE INFLUENCE."

SIR: Your account in the issue of January 24 of what was said at the meeting of the New South Wales Branch of the British Medical Association held on October 30, 1941, was of great interest, but what was even more interesting was what was not said.

Before I say any more, it should be stated that my outlook on the social aspects of alcohol is about average, and I am not influenced by the uncompromising views of "temperance" organizations. But what did surprise me was that no consideration was given at the meeting to the place that alcohol should assume in a planned national economy. Have not the alcohol interests exceeded their reasonable position in the community? That alcohol has a social value can be accepted, but what can be said in its favour on pharmacological or nutritional grounds? What contribution can it make to national fitness?

When we read advertisements which "educate" the public to: "Keep fit—drink somebody's beer" or: "Balance your diet—drink somebody's stout", is it not our function to point out the fallacy? Are these statements not deliberately misleading?

What effect has the national drink bill on the low consumption of milk in Australia? Is there not something fundamentally wrong in our national outlook when the retail alcohol trade carries on its business in the best building in the town, while human constructive agencies, such as kindergartens and health centres, have to catch the drips from the leaky roofs in any dish that is available?

I have had a personal demonstration of the power of the alcohol trade in "commercial censorship" applied to the newspapers and radio stations.

The government revenue produced by the alcohol trade gives it a privileged position in the community, while the discreet donations to party funds enable political power to be wielded. Are we fighting today to make Australia safe for the breweries?

These are basic aspects, but more germane to the problem of "driving under the influence" is the need for public education in the effect of alcohol on motor driving efficiency. Could not the British Medical Association and the police do this? Is it asking too much of the social sense of the alcohol interests to expect them to help?

Must we assume that alcohol consumption in Australia will continue to increase, and to extend our police and hospital services to meet the situation. These are some of the items that could be usefully included in the agenda of the subcommittee of the British Medical Association whose formation was projected at the meeting.

Yours, etc.,

NOEL M. GUTTERIDGE.

Inchcolm,
Wickham Terrace,
Brisbane.
February 6, 1942.

BURNS OF THE HANDS AND FINGERS.

SIR: Much has been written lately on this subject, as the incidence in war-time is high, and it is recognised that burns of the hands and fingers possess their own peculiar dangers. The tragic sequelae of loss of function, contractures, and even ultimate amputation are far too common, particularly after enthusiastic coagulation therapy. True, new methods have been evolved. We read of "Milton" (*The British Medical Journal*, July 12, 1941, page 46) and "Englamide", and long for something simple. The application of "Vaseline" gauze and "closed" plaster appears to be efficacious, but there remains in many minds a deep prejudice against immobilizing injured and infected fingers. There is, however, an old favourite (seldom advertised), whose simplicity and safety can hardly be questioned. I refer to treatment with boracic ointment dressings. This method has been used for some years in the Sydney Hospital casualty ward for this type of injury, and has never done any harm—a record not shared by many of its rivals. No doubt the principle is of more importance than the actual substance used, and other types of ointment may be just as efficacious. Boracic ointment is our choice, and gives good results. It can be obtained almost anywhere, and preparation is simple. *Ung. Acid. Boric.*, B.P., is smeared liberally onto sterile lint, which is then cut into one and a half inch strips. After cleansing the area gently and removing blebs, a strip is applied longitudinally to each finger, that is, along the dorsum, over the tip and back along the palmar surface. This eliminates constriction. The edges are then pressed together and the finger bandaged lightly. The hand and wrist are then dressed and a cock-up splint applied. The latter can usually be removed after forty-eight hours, when pain is slight or absent, and active movements started. Despite oozing of serum, it is important that dressings be changed as seldom as possible. Every fourth day will suffice, as the first principle in treating any burn after applying the initial dressing is to leave well alone. Oozing will stop in good time and can be taken up if necessary

by outer dressings. The skin tends to become white and thickened, but this will clear up when the dressings are discarded. The following case is cited as typical of this treatment.

On January 7 a soldier received petrol burns to both hands and thighs when a Bren gun carrier capsized. His comrades had poured flour generously over the burnt areas. Pain was severe when he was seen two hours later. On scraping off the resultant dough under anaesthesia, the right hand was found to be completely "degloved". The left was not so badly damaged, but all the fingers were "degloved". Underlying tissues were a deep red, and the burns appeared to be third degree. Boracic ointment dressings were applied in the manner described. Splints were removed on the third day and active movements started. The right dressing was changed on the fourth day and the left on the fifth, as the procedure was moderately painful. The areas were clean. After this the movements improved, and when these dressings were removed on the ninth day pain was absent and healing practically complete. Dressings were discarded altogether on the thirteenth day, and the skin softened twice daily with lanoline. There was no scarring or loss of movement. At this stage the tannic acid coagulum was still firmly adherent to both thighs and did not separate completely for another week. He has since returned to duty. Surely this simple "old-fashioned" method of treatment deserves wider publicity.

Yours, etc.,

P. W. GILL (Captain),
Medical Officer,
Military Hospital.

February 14, 1942.

AN APPEAL.

SIR: Would you kindly find space for an extract of a letter dated December 10, 1941, from Surgeon Rear-Admiral Cecil P. G. Wakeley, Royal Naval Hospital, Haslar, Gosport, Hants.

I wish you would help me with some of my anxiety-cases after repeated bombing. I find one way to keep these men busy is to get them to collect stamps and put them in albums—their proper places. So if you and your friends will send me all the used Australian, New Zealand or other stamps (used) I should be so glad. Don't soak the stamps off the paper, as this gives the patients something to do. We use every method we can think of to keep the men's minds occupied.

I am sure the many friends Mr. Wakeley formed on his visit to Australia a few years ago will be glad to help him.

Yours, etc.,

H. BULLOCK.

Sydney.

February 17, 1942.

Obituary.

WILLIAM GEORGE ARMSTRONG.

We are indebted to Dr. Cecil Purser for the following account of the career of the late Dr. William George Armstrong, whose death was announced recently in these pages.

William George Armstrong, who was born in England, came to Australia when he was about sixteen years of age. For a short time he acted as a member of the teaching staff of Sydney Grammar School. He then entered the University of Sydney, where he graduated as Bachelor of Arts in 1884. In 1885 he entered the medical school; this was the second year of the little old four-roomed medical school's existence. He graduated in 1888 as Bachelor of Medicine and Master of Surgery with the first batch of graduates in medicine. Since the graduands were called up alphabetically that year, W. G. Armstrong was called first; hence he was the first to graduate from the medical school of the University of Sydney. The late Peter Bancroft, of Brisbane, gold medallist of the first batch, had his degree conferred second. Armstrong was addressed as "W.G." to distinguish him from his brother Laurens, who graduated as Bachelor of Arts in the same year.

In our first curriculum the first year in the arts course and the first year in medicine were the same, and a graduate in arts entered the second year in medicine; hence "W.G." entered as a second-year undergraduate in 1885. The

medical school opened in 1883, but no one passed the final or fifth-year examination in 1887. The Reverend D. D. Rutledge, M.A., was the only one to do the fifth-year work again, and he graduated with the first batch in 1888. "W.G." was the last but one of the first batch of graduates to "cross the bar". Dr. L. Gordon Davidson is still with us.

After graduation "W.G." started general practice at Tingha, a tin-mining town in the north-west of New South Wales, where he stayed for a few years, and then he moved to Bowral to practise. He later proceeded to England and obtained the D.P.H. (Cambridge) in 1895. He returned to Sydney and was appointed medical officer for health for Sydney in 1898; he was city health officer from 1900 to 1912; he became director-general of public health and medical adviser to the Government in 1900 and retired from that position in 1924. He was afterwards appointed a member of the Board of Health and retained that position until his death.

We were undergraduates together in arts 1883 to 1884, and in medicine 1885 to 1888, and were co-workers together in the Health Department from 1920 until his last illness.

As an undergraduate he interested himself in general university work. He was very keen in the establishment of the University Boat Club and was really one of the founders of the club; and he was markedly interested in working that club all his undergraduate years.

As a lecturer and examiner in medical jurisprudence and public health at the Sydney University Medical School from 1904 to 1921, he did especially good work for the students of that period and assisted them markedly to obtain a good knowledge of their work. He was an excellent lecturer and demonstrator and was very helpful to his students.

From the date of his appointment as medical officer of health for Sydney, all through his term of office in the Health Department he showed great keenness and knowledge of his work in all the various ramifications of the department. He was a hard worker and carried out his duties with zeal and efficiency.

He was thorough and reliable, and was especially well versed in all matters pertaining to health. He did especially good work during the smallpox epidemic some years ago. He was a good raconteur and a most agreeable and likeable companion and co-worker. He certainly lived his life and carried out much good work pertaining to health for younger New South Wales. Those who were in close contact with him and his work will sadly miss his passing on.

Dr. E. Sydney Morris writes:

Dr. William George Armstrong, who was born in England, came to Australia when he was about sixteen years of age.

For a short time he was on the teaching staff of Sydney Grammar School, and later entered the university, where he acquired the degree of B.A. in 1884.

He was one of the first three graduates in medicine of Sydney University, graduating M.B., Ch.M. in 1888.

He was in general practice for varying periods until about the year 1895, when he went to England to obtain the Diploma of Public Health at Cambridge. Returning to Sydney after obtaining the D.P.H., he was appointed medical officer of health for Sydney, and in 1900 was, in addition, appointed city health officer. Subsequently, when the

metropolitan combined sanitary district was established, he became the medical officer of health and retained that position until 1913, when he was appointed deputy director-general of public health. In 1920 he was appointed director-general of public health and President of the Board of Health.

Health, retiring from the Public Service some four years

For about eighteen years he was lecturer and examiner in public health in the University of Sydney and was therefore personally known to many hundreds of medical practitioners whom he had taught as students. He was chairman or a member of numerous official boards and committees during his years of office, and after retirement retained his membership of the Board of Health until his death.

W. G. Armstrong was one of the pioneers of public health in Australia, and early in his career was actively engaged in the control of the serious outbreak of bubonic plague (1900-1901) in Sydney. He was certainly the first in the field in Australia, if not in the southern hemisphere, in concerted

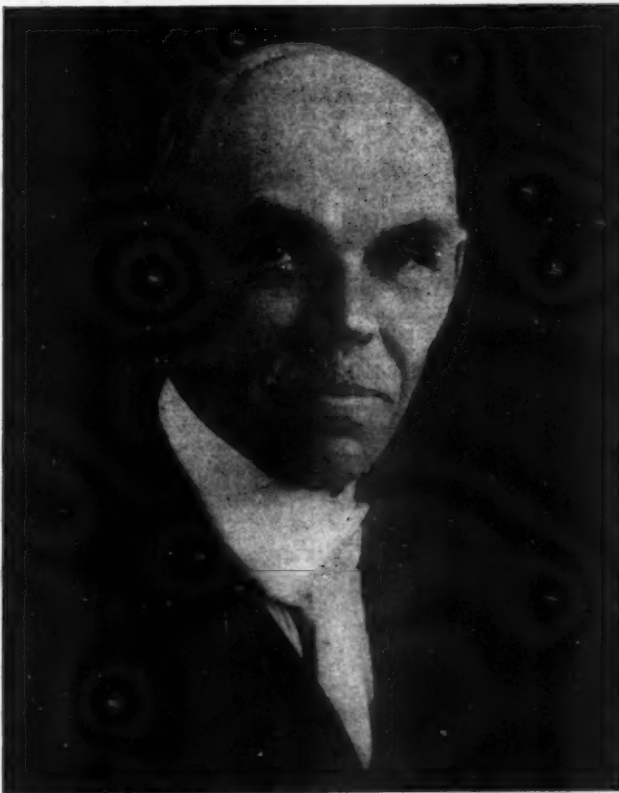
action for the reduction of infant mortality. It is frequently asserted that New Zealand was the first country in this part of the world to establish mothercraft training. In 1903, four years before any similar activity commenced in New Zealand, Dr. Armstrong issued a pamphlet, "Advice to Mothers", in which he strongly urged breast feeding as the greatest safeguard against gastro-enteritis, at that time the outstanding cause of infant mortality. A copy of this pamphlet was sent to every address at which a birth had been registered.

The following year he succeeded in obtaining the appointment of a trained health visitor to visit the mothers of all newly born babies in the city of Sydney. Some six years later he was instrumental in extending the work beyond the city to the more populous of the metropolitan suburbs. The first baby health centre in New South Wales was established in 1914, and from this beginning the centres have spread practically throughout the State. The great reduction of infant mortality effected in the past forty years can, I think, be ascribed in large measure to the efforts and influence of our late colleague.

Dr. Armstrong contributed many excellent articles on public health and preventive medicine to various journals. Some of his best contributions are contained in the official "Annual Reports of the Director-General of Public Health" (New South Wales), in which he deals with the epidemiology of bubonic plague, smallpox, influenza *et cetera* from first-hand field experience.

Though he reached an age well beyond the allotted span, he was never a robust man. This, however, did not impede his enthusiastic and untiring efforts for the improvement of the public health, which remained a dominant incentive and professional ideal throughout his long life. I did not have the privilege of working with Dr. Armstrong as an official colleague. Our relationship, during his official career, was rather that of teacher and disciple; but I am deeply indebted for his help as "guide, philosopher and friend" during a period of thirty years.

He was a magnanimous man, an outstanding administrator, a gentleman under all circumstances, and a practitioner actuated throughout his long life by the highest ideals of his profession. He has left his mark on the Department of Public Health of New South Wales, in which his reputation is a spur and inspiration to his successors. In the ultimate



analysis a man's true worth can only be assessed on the basis of whether the world is better for his having lived therein. On that basis it can be definitely asserted that W. G. Armstrong was weighed in the balance and found not wanting.

JONATHAN PERCY MOSS BLACK.

We regret to announce the death of Dr. Jonathan Percy Moss Black, which occurred on February 16, 1942, at Dromana, Victoria.

University Intelligence.

THE UNIVERSITY OF CAMBRIDGE.

Diploma in Medical Radiology and Electrology.

THE Committee for the Diploma in Medical Radiology and Electrology gives notice that the University of Cambridge has decided that the regulations for the diploma in medical radiology and electrology will be rescinded on October 31, 1943, and that no examination will be held and no diplomas granted after that date. The course which started in October, 1941, is therefore the last course that will be given for the diploma.

Australian Medical Board Proceedings.

NEW SOUTH WALES.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Practitioners Act, 1933-1939*, of New South Wales, as duly qualified medical practitioners:

Puleston-Jones, Eluned Myfanwy, M.R.C.S. (England), L.R.C.P. (London), 1931, Moss Vale Road, Bowral.
O'Grady, James Joseph, M.B., B.Ch., 1923 (Univ. Dublin), Union Bank of Australia Limited, Pitt and Hunter Streets, Sydney.

Walkingshaw, Richard, M.B., Ch.B., 1923 (Univ. Glasgow), 1937, F.R.C.S. (Edinburgh), Bank of New South Wales, George Street, Sydney.

Friedman, Icyk Mayer, 23, Adelaide Street, Bellevue Hill. Registered in accordance with the provisions of section 17A of the *Medical Practitioners Act, 1933-1939*.

Delbridge, Dorothy, M.B., Ch.B., 1923 (Univ. Bristol), Methodist Missionary Training College, 5, Roger's Avenue, Haberfield.

Pearlman, Eugene Nathaniel, M.R.C.S., 1936 (England), L.R.C.P. (London).

The following additional qualification has been registered: Kenny, Rawdon Hamilton (M.B., B.S., 1923 (Univ. Sydney), M.S., 1941 (Univ. Sydney), Rose Bay.

The following change of name has been registered.

Whiddon, Helen Maude, Manildra, M.B., B.S., 1933 (Univ. Sydney), name now Row, Helen Maude.

Nominations and Elections.

THE undermentioned have been elected members of the South Australian Branch of the British Medical Association:

Betts, William James, M.B., B.S., 1941 (Univ. Adelaide), Royal Adelaide Hospital, Adelaide.

Lyons, Henry Emerson Wescombe, M.B., B.S., 1941 (Univ. Adelaide), 198, Wellington Square, North Adelaide.

Corrigendum.

IN an article by F. H. Mills on hepatic function in thyrotoxicosis published in the issue of February 14, 1942, by a printer's error a wrong line was inserted in the third paragraph on page 198. The sentences in the third, fourth and fifth lines should read: "In severe cases good liver function readings may be obtained. In this series . . ." In the second and third lines from the bottom of the column the words "the liver function" should read "this liver function test".

Medical Appointments.

Dr. William Edward Lodewyk Hamilton Crowther has been appointed to the Millbrook Home Board, Tasmania, in pursuance of the provisions of Section 4 of the *Psychopathic Hospital (Management) Act, 1933*.

Dr. William John Freeman has been appointed an Official Visitor to the Lachlan Park Hospital, New Norfolk, Tasmania, in pursuance of the provisions of the *Insane Persons Hospitals Amendment Act, 1885*.

Diary for the Month.

MAR. 4.—Western Australian Branch, B.M.A.: Council.
MAR. 5.—South Australian Branch, B.M.A.: Council.
MAR. 6.—Queensland Branch, B.M.A.: Branch.
MAR. 10.—Tasmanian Branch, B.M.A.: Branch.
MAR. 13.—Queensland Branch, B.M.A.: Council.
MAR. 18.—Western Australian Branch, B.M.A.: Branch.
MAR. 24.—New South Wales Branch, B.M.A.: Council Quarterly.
MAR. 26.—New South Wales Branch, B.M.A.: Annual Meeting.
MAR. 26.—South Australian Branch, B.M.A.: Branch.
MAR. 27.—Queensland Branch, B.M.A.: Council.
MAR. 27.—Tasmanian Branch, B.M.A.: Council.
MAR. 31.—New South Wales Branch, B.M.A.: Council.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 155, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmal United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phoenix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia.

Editorial Notices.

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All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility unless such a notification is received within one month.

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